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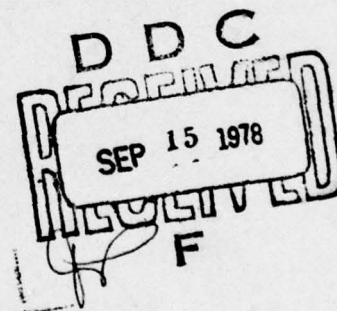
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**RADIATION EMESIS REPOSITORY (1971-1977):  
AN ANALYSIS**

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USAF SCHOOL OF AEROSPACE MEDICINE  
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# NOTICES

This final report was submitted by personnel of the Weapons Effects Branch, Radiation Sciences Division, USAF School of Aerospace Medicine, Aerospace Medical Division, AFSC, Brooks Air Force Base, Texas, under job order 7757-05-18.

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The animals involved in this study were procured, maintained, and used in accordance with the Animal Welfare Act of 1970 and the "Guide for the Care and Use of Laboratory Animals" prepared by the Institute of Laboratory Animal Resources - National Research Council.

This report has been reviewed by the Information Office (OI) and is releasable to the National Technical Information Service (NTIS). At NTIS, it will be available to the general public, including foreign nations.

This technical report has been reviewed and is approved for publication.

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20. ABSTRACT (Continue on reverse side if necessary and identify by block number) Emesis data collected from 21 ionizing radiation studies involving 210 rhesus ( <u>Macaca mulatta</u> ) monkeys has been examined. These studies contain a wide variety of experimental parameters prepared by investigators interested in unique situations. When proposed, they were viewed as pilot studies to determine the presence or the absence of radiation effects upon performance. This report examines the studies <u>a posteriori</u> grouping them as follows: Distribution Specification, (ED 50) Determinations, Dose Rates, Mixed Rates, and Descriptive. ED 50 SUB 50			

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20. ABSTRACT (Continued)

Distribution specification studies found that the onset time of each episode had an exponential distribution, and the duration of each episode was either an exponential or Weibull distribution. The presence of similar distributions across many experiments suggests that the same mechanism is at work in each study and episode, differing only in intensity. ED<sub>50</sub> studies found the effective dose for 50% emetic response to be 446 rads (Co<sup>60</sup>, 20 rads/min), and that motion reduced the ED<sub>50</sub> to 258 rads. Dose rate studies indicate a requirement for at least 10 animals per treatment group in making intergroup comparisons. Mixed rate and descriptive studies indicate the need for more systematic investigations. In an average rhesus monkey, if emesis occurred, the first episode occurred at 40 min postirradiation, followed in about 15 min by a second episode, and in another 15 min by a third and last episode.

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## RADIATION EMESIS REPOSITORY (1971-1977): AN ANALYSIS

### INTRODUCTION

This report summarizes the contents of the USAF School of Aerospace Medicine Radiation Sciences Division ionizing emetic repository from 1971 to 1977. This period includes the 21 studies listed in Table 1. As a group, the studies contain a wide variety of experimental parameters prepared by different investigators interested in unique and sometimes specified situations, and emesis data was collected incidental to the primary objectives of their experiment. Nevertheless, the emesis data can be viewed as pilot studies reflecting on this common syndrome, recognizing that the experiments were not designed for elaborate modeling efforts. With this in mind, we grouped the studies a posteriori on the basis of the analysis permitted by the data collected as follows:

Distribution specification (Studies 2, 18, 19, 27, 30, 33)  
ED<sub>50</sub> determinations (Studies 39, 41)  
Dose rates (Studies 31.1, 31.2)  
Mixed rates (Studies 36, 37, 38, 40)  
Descriptive (Studies 3.1, 3.2, 26, 28, 32, 34, 35)

Computer programs used to examine this repository are documented to provide continuity to this data base. Brief explanations are given so nonprogrammers can access the data to update and/or pursue additional analysis.

We use the operational definition of emesis given by Fleischman and associates (4). That is, an emetic episode is defined as a "series of three or more reflexive movements consisting of coordinated mouth openings, opisthotonus, and maximal abdominal musculature contraction." Interepisode time is defined as "3 or more minutes between the last emetic movement of an episode and the first emetic movement of the subsequent episode." Note that this definition includes both productive and nonproductive episodes. This is necessary because monkeys have cheek pouches and can conceal or retain vomitus. Thus it is intended to indicate when the subjects are distressed beyond the stage of nausea. Appendix A illustrates this definition by graphically portraying the temporal nature of the emetic responses for subjects in the repository. Sources of variation evident in these figures include:

- a. Whether or not a subject will experience an emetic episode.
- b. Number of episodes experienced if there is emesis.

TABLE 1. CONTENTS OF THE ENETIC REPOSITORY (1971-1977)

Study	Date	No. subjects	Weight kg	Hours observed	Task	Hours fasted	Exposure site	Type radiation	Neutron-gamma ratio	Delivery mode	Total mid-epigastric dose
2	3/72	16	2.0-3.1	15	D-	17	AMM	N/G	.72	2 Pulse	2160-2650
3.1	10/71	6	3.3-6.8	2	LAND	1.3, 1.6	AMM	N/G	.5	Sep. by 10m	600-1000
3.2	10/71	6	3.2-6.8	2	LAND	1.1, 1.6	AMM	N/G	.5	1 Pulse	600-1000
18	7/71	11	3.2-4.1	22	PEP	1.14	AFPRI	N/G	.24	Steady rate	1020-2920
19	3/72	9	2.3-3.7	22	PEP	1	AMM	N/G	.5	1 Pulse	2840-3380
26	8/72	9	3.0-5.0	2	PEP	17	AMM	N/G	.65	1 Pulse	283-2224
27	8/72	19	3.2-3.7	2	D-	17	AMM	N/G	.44	1 Pulse	2122-2365
28	3/73	10	3.2-4.3	2	PEP	1	AMM	N/G	.5	1 Pulse	170-1110
30	10/73	12	3.6-5.8	2	D-	1	SAM	X-ray	N/A	Steady rate	341-528
31.1	5/71	12	2.7-3.4	2	NAIVE	1.6	SAM	X-ray	N/A	Steady rate	517-580
31.2	5/71	12	2.8-3.5	2	NAIVE	1.6	SAM	X-ray	N/A	Steady rate	539-573
32	7/71	12	2.5-3.1	2	NAIVE	1	AFPRI	N/G	.24	1 Pulse	950-1130
33	9/71	4	3.0-3.4	2	NAIVE	1	SAM	X-ray	N/A	Steady rate	883-995
34	1/72	12	3.0-4.4	2	NAIVE	1.6	WEXR	N/G	5.0	1 Pulse	470-1000
35	3/74	10	?	2	PEP	1	AMM	N/G	?	?	250-500
36	12/75	8	2.95-4.32	12	D-	1	SAM	Co60	N/A	Mixed rates	300-300
37	12/75	7	2.95-4.32	12	D+	1	SAM	Co60	N/A	Mixed rates	300-300
38	12/76	4	4.3-5.7	72	PEP	1	SAM	Co60	N/A	Mixed rates	300-300
39	3/77	15	4.4-6.5	4	NAIVE	1	SAM	Co60	N/A	Steady rate	350-550
40	12/76	10	4.4-5.7	10	PEP/MART	1	SAM	Co60	N/A	Mixed rates	1440-1440
41	4/77	6	5.0-5.9	4*	SHAKE	1	SAM	Co60	N/A	Steady rate	200-300

D- = Lever pressing; Shock reinforcement  
 D+ = Lever pressing; Food reinforcement  
 LAND = Landolt  
 PEP = Primate equilibrium platform  
 NAIVE = No behavioral laboratory experience  
 PEP/MART = Primate equilibrium platform  
 Multiple alternative reaction task  
 N/A = Not applicable

SHAKE = Motion  
 AMM = Texas AMM  
 N/G = Mixed neutron-gamma radiation  
 SAM = School of Aerospace Medicine  
 WEXR = White Sands Missile Range  
 AFPRI = Armed Forces Radiobiological Research Institute  
 ? = Unknown  
 \* = Observed until first episode; if no emesis, then 4 h

c. Kinds of episodes experienced (productive vs. nonproductive).

d. Duration of episodes.

e. Time of occurrence of each episode.

#### DISTRIBUTION SPECIFICATION (Studies 2, 18, 19, 27, 30, 33)

##### Methods

The approach used in modeling the prodromal syndrome is that used in the analysis of reliability and life data. The reliability of each subject is the infrequency with which he experiences emesis. Our goal was to estimate the probability of a failure--an emetic episode as well as the time until it occurs, and the duration of the episode. The decision tree in Figure 1 illustrates this approach. The origin represents immersion in the radiation field. The probability of experiencing a first episode is  $p_1$ ; it takes  $t_1$  minutes to occur, and will last  $d_1$  minutes. The probability of a second episode is  $p_2$ ; it occurs  $t_2$  minutes following the first episode, and will last  $d_2$  minutes. This process continues until the last episode when  $p_{last+1} = 0$ . In this manner, the prodromal syndrome is viewed as a stochastic process.

For a given study, let  $n$  equal the total number of animals in the study and let  $x_i$  be the number of emetic responders during episode  $i$ . An estimate of  $p_i$  is  $\hat{p}_i = x_i/n$ .<sup>1</sup> Confidence intervals for  $p_i$  can be constructed from the binomial distribution (cf. ref. 12).

---

<sup>1</sup>As stated, the definition of  $p_i$  is vague. The modeler must decide upon the interpretation he wants to make. Let  $y_i$  represent the number of animals that have exactly  $i$  emetic responses.  $y_i = x_i - x_{i+1}$ . Related parameters are suggested by the additional estimates:

a.  $\tilde{p}_i = y_i/n = (x_i - x_{i+1})/n$ ; ( $x_0 = n$ )

b.  $\bar{p}_i = x_i/x_{i-1}$ ; ( $x_0 = n$ ).

$\tilde{p}_i$  is the probability of having exactly  $i$  episodes. Beta-binomial confidence limits can be constructed for these probabilities as described above with  $y_i$  replacing  $x_i$ .  $\bar{p}_i$  is a conditional probability which is the proportion of previous episode responders that respond again. Confidence limits using this estimate can be constructed from life table techniques. Unfortunately, these methods require relatively large sample sizes for meaningful intervals. Estimates for  $\tilde{p}_i$  and  $\bar{p}_i$  can readily be constructed from estimates for  $\hat{p}_i$  in Table 2. To avoid confusion, we limit future discussion to  $\hat{p}_i$ .

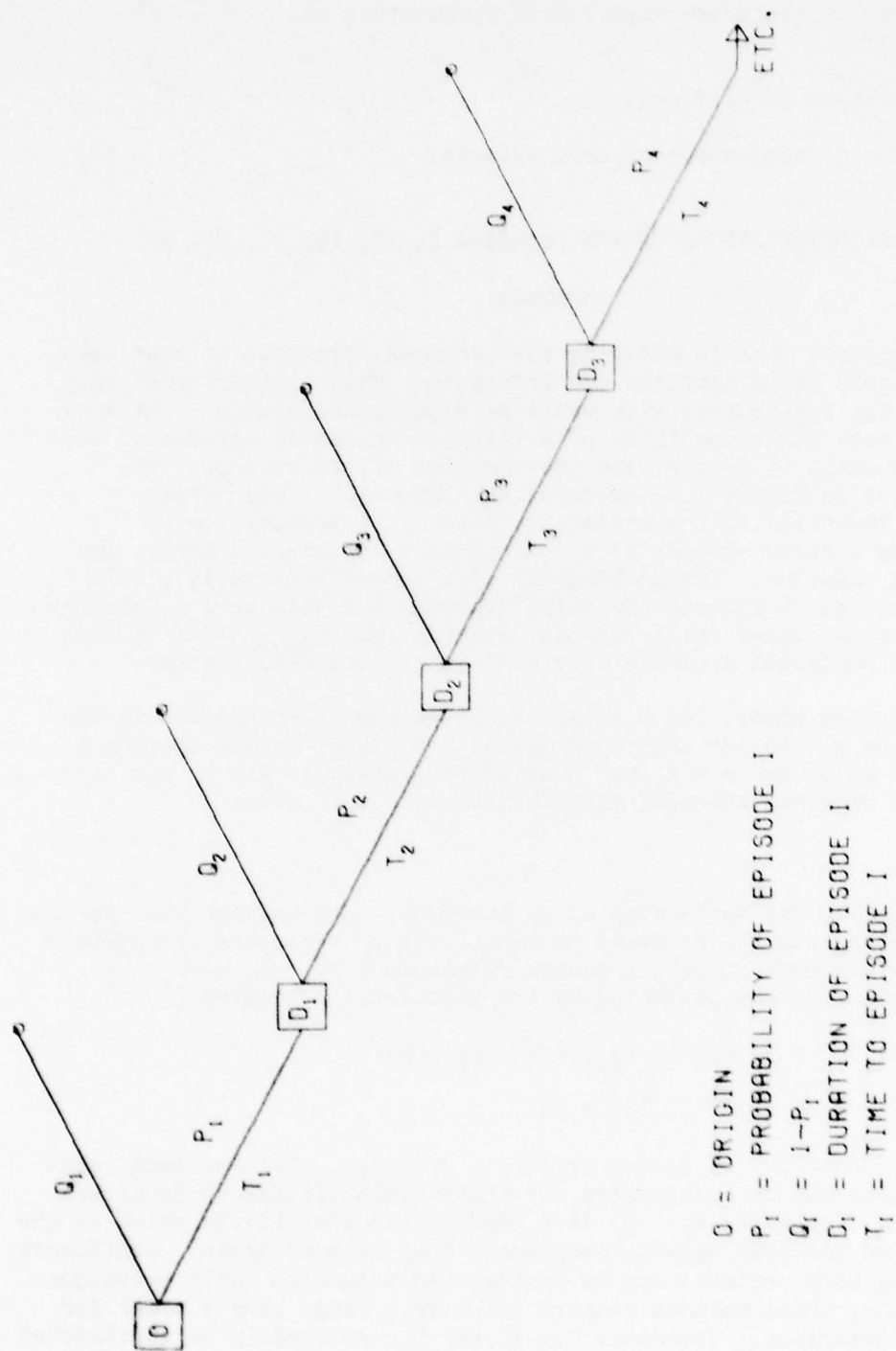


Figure 1. Decision tree for the prodromal syndrome.

The approach to determining  $t_i$  and  $d_i$  was to consider them as random variables  $T_i$  and  $D_i$  whose distributions need specification. With small sample sizes, customary  $\chi^2$ -goodness-of-fit tests are inappropriate for distribution determination as are the Kolmogorov-Smirnov (KS) tests which require a priori knowledge of parameters. We examined two of the most frequently occurring distributions in life testing--the exponential and the Weibull. These densities are given by:

$$f_X(x) = \frac{1}{\lambda} \exp\left(-\frac{1}{\lambda}x\right), \quad x > 0$$

$$= 0, \quad x \leq 0$$

for the exponential, and

$$f_X(x) = \frac{\beta}{\delta} \left(\frac{x-\mu}{\delta}\right)^{\beta-1} \exp\left[-\left(\frac{x-\mu}{\delta}\right)^\beta\right], \quad x \geq \mu$$

$$= 0, \quad x < \mu; \quad \beta, \delta > 0; \quad \mu \geq 0$$

for the Weibull. With  $\beta = 1$  and  $\mu = 0$ , one can see that the exponential is a special case of the Weibull. To test the adequacy of the exponential, we used a modified KS technique given by Lilliefors (5) for samples  $\geq 3$  and by Finklestein and Schafer (3) for samples = 2. A test derived by Mann, Scheuer, and Fertig (9) was used to test the adequacy of a two-parameter Weibull distribution ( $\mu = 0$ ) when the exponential distribution failed. All testing was done at the  $\alpha = .01$  level. Following selection of a distribution, maximum likelihood estimates were used to estimate exponential parameters; Mann's (7, 8) best linear invariant estimates were used for  $\beta$  and  $\delta$  estimates in Weibull distributions.

## Results

Tables 2 and 3 classify, respectively, by study and episode the proportion of emetic responders and the 95% confidence intervals for these proportions. The width of the confidence intervals in Table 3 is a function of the sample size and the  $\alpha$ -level considered. Despite their width, meaningful data can still be gleaned by examining the end points of these intervals. For instance, the lower limits for  $p_1$  in studies 2 and 27 indicate that at least 47% and 43% of those respectively exposed to such dose profiles (and associated experimental parameters) would experience the prodromal syndrome. Information of this nature could thus be used to make best-case inferences. By the same token upper limits for  $p_3$  in study 30 indicate that, at most, 41% of those exposed to these experimental conditions would experience 3 episodes, while upper limits for  $p_4$ - $p_8$  indicate that a maximum of 23% will have 4 or more emetic episodes. Worst-case estimates can thus be made from these upper limits. Both best- and worst-case estimates from

TABLE 2. PROPORTION ( $\bar{p}_i$ ) OF ENETIC RESPONDERS (PRODUCTIVE AND NONPRODUCTIVE)

Study	Episode							
	1	2	3	4	5	6	7	8
2	12/16	11/16	9/16	6/16	2/16	1/16	1/16	0/16
18	4/7	2/7	1/7	0/7	0/7	0/7	0/7	0/7
19	5/9	3/9	1/9	1/9	1/9	0/9	0/9	0/9
27	13/19	10/19	6/19	3/19	1/19	1/19	1/19	1/19
30	5/11	2/11	1/11	0/11	0/11	0/11	0/11	0/11
33	3/4	2/4	1/4	1/4	1/4	0/4	0/4	0/4

TABLE 3. PROBABILITY OF HAVING AN ENETIC RESPONSE (95% CONFIDENCE INTERVALS)

Study	Episode							
	1	2	3	4	5	6	7	8
2	(.47, .93)	(.41, .89)	(.29, .81)	(.25, .65)	(.01, .38)	(0.0, .30)	(0.0, .30)	(0.0, .27)
18	(.18, .90)	(.03, .71)	(0.0, .58)	(0.0, .33)	(0.0, .25)	(0.0, .35)	(0.0, .35)	(0.0, .35)
19	(.21, .86)	(.07, .70)	(0.0, .48)	(0.0, .48)	(0.0, .48)	(0.0, .28)	(0.0, .28)	(0.0, .28)
27	(.43, .87)	(.28, .76)	(.12, .57)	(.03, .40)	(0.0, .26)	(0.0, .26)	(0.0, .26)	(0.0, .26)
30	(.16, .77)	(.02, .52)	(0.0, .41)	(0.0, .23)	(0.0, .23)	(0.0, .23)	(0.0, .23)	(0.0, .23)
33	(.19, .99)	(.06, .93)	(0.0, .81)	(0.0, .81)	(0.0, .81)	(0.0, .53)	(0.0, .53)	(0.0, .53)

Table 3 are based upon 95% confidence limits. If one wanted to be less secure in these estimates, the confidence intervals could be shortened by increasing the  $\alpha$ -level.

Tables 4 and 5 summarize by study and episode the distributions selected to describe  $T_1$  and  $D_1$  based upon  $\alpha = .01$ . In all (17 of 17) cases where the distributions could be identified, the distributions of time to failure ( $T_1$ ) were exponentially distributed. This distribution suggests that when the prodromal syndrome occurs, one can characterize when it will happen as a function of  $\lambda$  which is dependent upon experimental conditions like hours fasted, radiation type, and the neutron-gamma ratio. Estimates of  $\lambda$  are informative, and they represent the mean time between failures. In all cases, we find that it takes longer for the first episode to occur than for successive episodes.

In 13 of 17 cases, the exponential distribution was an adequate descriptor of episode duration times at the .01 level. The Weibull was able to describe an additional 2 cases. The remaining 2 cases were neither Weibull nor exponential and are unknown. With  $\mu = 0$ , we can describe 15 of 17 cases of  $D_1$ 's distribution as belonging to a two-parameter Weibull family. This characterization suggests that episode duration times can be described as functions of  $\beta$  and  $\delta$  which depend upon experimental conditions. Thus, the same mechanism appears to be at work in each study and episode, but differing only in intensity. Estimates of  $\lambda$  (for the exponential subclass) are mean duration times for each episode. Study 2 with the greatest incidence, the most episodes, and the shortest time to the first episode appears to have the greatest duration times on the average.

#### Comments

The diversity of experimental parameters suggests a number of hypotheses to be tested. For a given dose, they include the hypothesis of

- a. No difference between the same dose delivered as a single pulse vs. a double pulse, or a single pulse vs. a continuous dose rate, etc.
- b. No difference between different dose rates.
- c. No difference between fasting animals 17 h, 6 h, or 1 h.
- d. No difference between behavioral tasks (PEP, D+, D-, Landolt, Naive).
- e. No difference between .25, .50, or .75 neutron-gamma ratios.

With hindsight, one would like to test each of these hypotheses. Given the current situation, none can be examined because no two of the several studies differ in only a single independent variable.

TABLE 4. MEAN ONSET TIMES FOR EPILEPTIC EPISODES IN MINUTES  
(Distribution specification for  $T_1$ ;  $\sigma = .01$ ;  $\lambda =$  Mean time to onset in minutes)<sup>a</sup>

Study	Episode							
	1	2	3	4	5	6	7	8
2	$\lambda = 11.81b$	$\lambda = 10.78$	$\lambda = 11.13$	$\lambda = 15.69$	$\lambda = 11.5$	N=1	N=1	N=0
18	$\lambda = 43.4$	$\lambda = 27.25$	N=1	N=0	N=0	N=0	N=0	N=0
19	$\lambda = 30.43$	$\lambda = 9.38$	N=1	N=1	N=1	N=0	N=0	N=0
27	$\lambda = 28.92$	$\lambda = 17.48$	$\lambda = 9.17$	$\lambda = 10.31$	N=1	N=1	N=1	N=1
30	$\lambda = 53.13$	$\lambda = 12.02$	N=1	N=0	N=0	N=0	N=0	N=0
33	$\lambda = 42.58$	$\lambda = 18.56$	N=1	N=1	N=1	N=0	N=0	N=0

<sup>a</sup>  $\lambda$  indicates an exponential distribution.  $\delta$  and  $\beta$  indicate a Weibull distribution. N = 1 or N = 0 indicate sample sizes preventing distribution specification. Question marks (?) indicate that neither the Weibull nor the exponential could describe these cases with  $\sigma = .01$ .

<sup>b</sup> Time since second pulse, which occurred 10 min after first pulse.

TABLE 5. DURATION OF EPILEPTIC EPISODES IN MINUTES  
(Distribution specification for  $D_1$ ;  $\sigma = .01$ ;  $\lambda =$  Mean duration time)<sup>a</sup>

Study	Episode							
	1	2	3	4	5	6	7	8
2	$\lambda = 3.24$	?	$\lambda = 4.19$	$\lambda = 3.3$	$\lambda = 3.55$	N=1	N=1	N=0
18	$\lambda = 2.58$	$\lambda = 4.1$	N=1	N=0	N=0	N=0	N=0	N=0
19	$\lambda = .48$	$\lambda = .39$	N=1	N=1	N=1	N=0	N=0	N=0
27	$\lambda = 2.13$	$\delta = 3.62$	$\beta = 13.40$ ; $\lambda = 1.86$	$\lambda = 1.56$	N=1	N=1	N=1	N=1
30	?	$\lambda = .84$	N=1	N=0	N=0	N=0	N=0	N=0
33	$\delta = 2.45$ ; $\beta = 71.78$	$\lambda = 3.66$	N=1	N=1	N=1	N=0	N=0	N=0

<sup>a</sup> See footnote a, Table 4.

Another consideration could be to shorten the range of total midepigastic doses for a given study. In study 18, 4 animals in the 1000-rad dose range were deleted from consideration in distribution specifications. This left 7 animals in the dose range of 2440-2990 rads. It is preferable to make inferences over narrow dose ranges, say 25-50 rads, rather than over a 550-rad range. This variability in dose ranges affects the precision of  $p$ ,  $p_u$ ,  $p_{ui}$ ,  $\lambda$ ,  $\delta$ , and  $\beta$ . Additionally, these estimates can be improved by increasing the sample sizes in each study.

#### ED<sub>50</sub> DETERMINATIONS (Studies 39, 41)

##### Methods

The ED<sub>50</sub> number is the effective dose for which 50% of a population will have an emetic episode. A literature search showed that estimates exist for humans, but none could be found for monkeys. We therefore sought to fill this void to aid in monkey-to-man extrapolations. The up-and-down method (1, 2) was selected over probit techniques because accurate estimates could be obtained with smaller samples. The procedure was to administer doses at equally spaced increments. If the primate vomited, the increment was lowered one unit. If the primate did not vomit, the dose was raised one unit. The increment selected was 50 rads. Assumptions upon which the procedure is based include:

- a. Data is normally distributed with common variance.
- b. Subjects that do not vomit would have vomited at a sufficiently higher dose.

Advantages of this procedure are that it concentrates testing near the mean and can save in the number of subjects tested.

##### Results

The ED<sub>50</sub> for unrestrained man is reported to be 183 rads (log-normal distribution) or 214 rads (normal distribution) (6). Estimated ED<sub>50</sub> for naive, stationary, chair-restrained rhesus monkeys was 446 rads. Naive monkeys that were oscillated forward and backward  $\pm 5^\circ$  to  $10^\circ$  (pitch axis on the PEP) from horizontal had an ED<sub>50</sub> of 258 rads. Dose rate was 20 rads/min to simulate common radiation therapy dose rates from which human ED estimates were derived. Experimental results are given in Tables 6 and 7. Large and small sample ED<sub>50</sub> estimates are given in Tables 8 and 9. Note the close agreement of estimates by both large and small sample techniques. A comparison between stationary and motion groups is in order. This is accomplished via a large sample z-test.

TABLE 6. STATIONARY TREATMENT DATA

Dose (rads)	Subject														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
350	0 <sup>a</sup>				0										
400		0		x <sup>b</sup>		0						0			
450			x				0				x		0		x
500								0		x					x
550									x						

<sup>a</sup>0 = emetic nonresponder  
<sup>b</sup>x = emetic responder

TABLE 7. MOTION TREATMENT DATA

Dose (rads)	Subject					
	1	2	3	4	5	6
200					0 <sup>a</sup>	
250		0		x <sup>b</sup>		0
300	x		x			

<sup>a</sup>0 = emetic nonresponder  
<sup>b</sup>x = emetic responder

TABLE 8. LARGE SAMPLE ESTIMATES (cf. ref. 1)

Group	$N_0$	$N_x$	d (rads)	$ED_{50}$ (rads)	$S_x$ (rads)
Stationary	8	7	50	446.43	27.04
Motion	3	3	50	258.33	18.64

TABLE 9. SMALL SAMPLE ESTIMATES (cf. ref. 2)

Group	N	N'	d (rads)	$ED_{50}$ (rads)
Stationary	15	14	50	445.63
Motion	6	6	50	258.45

$$Z = \frac{\bar{X}_{\text{stationary}} - \bar{X}_{\text{motion}}}{\sqrt{\frac{S_{\text{stationary}}^2}{N_{\text{stationary}}} + \frac{S_{\text{motion}}^2}{N_{\text{motion}}}}} = \frac{446.43 - 258.33}{\sqrt{(27.04)^2 + (18.64)^2}} = 5.514$$

and is significant at the 5% level. We conclude that the presence of motion can trigger vomiting at lower doses.

#### Comments

The up-and-down technique uses substantially fewer monkeys than probit techniques, and should be considered in radiation studies designed to study effects of fasting on  $ED_{50}$  and/or the combined effects of radiation plus stressors other than motion.

Up-and-down step sizes should be about one standard deviation in magnitude, which approximates 70 rads for naive, stationary monkeys, and 30 rads for naive monkeys experiencing motion stress.

This monkey  $ED_{50}$  emesis data indicates a difference in radiosensitivity between man and monkey ( $ED_{50} = 183$  rads for man and 446 rads for partially restrained monkeys). Monkey-man extrapolation is apparently not 1 to 1, and deserves further study.

## DOSE RATES (Studies 31.1, 31.2)

### Methods

Study 31 involves subjects receiving approximately the same total midepigastic dose at 1 of 6 different dose rates and 1 of 2 different fasting schedules. These fasting schedules were designed to test the null hypotheses that

- (a) Fasting does not affect emesis.
- (b) Dose rates do not affect emesis.

Midepigastic doses ranged from 517 to 573 rads. Table 10 summarizes the data collected from each of 9 separate variables. Onset is the time in minutes to the first episode, with time accumulating from the moment the x-ray machine was turned on. Offset is the time in minutes at the conclusion of the last episode. Total duration is the total time in minutes that the subject experienced both productive and nonproductive emetic episodes. The period between onset and offset times is defined as the subject's vulnerability period. The definitions of the remaining 5 variables are self explanatory. Figure 2 shows mean plots for this data.

### Results

Hypothesis testing was accomplished by a two-factor analysis of variance. In all cases there were no significant dose rate x fasting interactions. Significant dose rate effects ( $p < .1$ ) were identified for onset and offset times, duration time of productive episodes, as well as the number of productive and nonproductive episodes. Significant fasting effects ( $p < .1$ ) were found for onset times and nonproductive duration times. Tukey's (cf. 11) multiple comparison procedure detected the following differences at the 10% level of significance.

- a. Onset and offset times for 6 rads/min dose rate were longer than both the 50 rads/min and 175 rads/min rates.
- b. Offset times at 12 rads/min were longer than at 175 rads/min.
- c. Productive duration times for 12 rads/min were longer than at 25 rads/min.
- d. The number of productive episodes at 12 rads/min were greater than at 25 rads/min.
- e. The number of nonproductive episodes at 25 rads/min were greater than at 12 rads/min.

TABLE 10. DOSE RATE DATA

Variable	Dose rate (rads/min)						Hours fasted
	6	12	25	50	92	175	
Onset	86.17	144.07	92.72	32.70	107.00	71.35	1
	136.67	97.17	72.07	52.25	43.13	46.45	1
	103.42	50.58	81.63	51.62	63.73	30.00	6
	101.55	67.55	54.23	31.55	90.07	47.02	6
Offset	122.08	168.23	93.15	119.64	107.08	83.96	1
	140.97	105.37	121.15	82.55	121.60	48.07	1
	127.46	121.62	121.76	90.80	64.21	46.03	6
	164.93	143.05	66.95	35.32	93.45	50.24	6
Vulnerability	35.91	24.16	0.43	86.94	0.08	12.61	1
	24.04	71.04	40.13	39.18	0.48	16.03	1
	4.3	8.2	49.08	30.3	78.47	1.62	6
	63.38	75.5	12.72	3.77	3.38	3.22	6
Total duration	2.87	11.65	0.43	8.93	0.08	4.23	1
	4.30	5.13	0.82	3.14	8.63	1.62	1
	6.68	10.29	4.78	8.35	0.48	7.70	6
	12.82	3.40	3.95	3.77	3.38	3.22	6
Productive duration	2.87	11.65	0.0	8.25	0.0	4.23	1
	4.30	5.13	0.0	3.14	7.08	1.62	1
	6.68	9.36	0.60	8.35	0.0	3.52	6
	7.47	3.40	0.0	0.0	0.0	3.22	6
Nonproductive duration	0.0	0.0	0.43	0.68	0.08	0.0	1
	0.0	0.0	0.82	0.0	1.55	0.0	1
	0.0	0.93	4.18	0.0	0.48	4.18	6
	5.35	0.0	3.95	3.77	3.38	0.0	6
Total number episodes	4	3	1	5	1	2	1
	1	2	2	2	4	1	1
	3	6	4	3	1	3	6
	5	2	2	1	1	1	6
Number productive episodes	4	3	0	4	0	2	1
	1	2	0	2	2	1	1
	3	5	1	3	0	1	6
	3	2	0	0	0	1	6
Number nonproductive episodes	0	0	1	1	1	0	1
	0	0	2	0	2	0	1
	0	1	3	0	1	2	6
	2	0	2	1	1	0	6

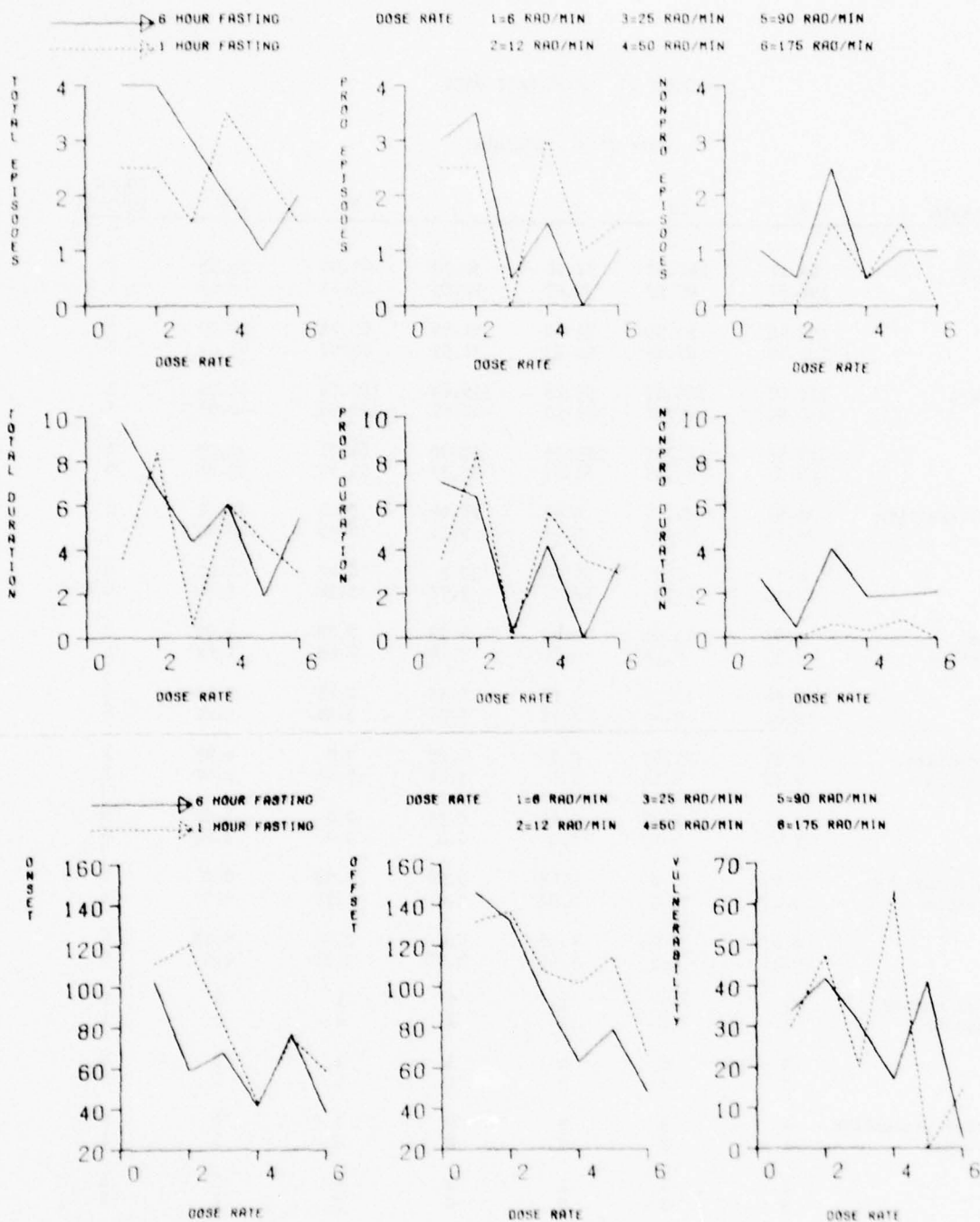


Figure 2. Mean scores for studies 31.1 and 31.2.

Note the lack of a clear-cut pattern in significant findings. For instance, if onset and offset times for 6 rads/min were significantly longer than both the 50 rads/min and 175 rads/min rates, one would have also expected them to be longer than the 92 rads/min rate. Similarly, if the number of nonproductive episodes at 25 rads/min were greater than at 12 rads/min, then one would have expected the number of nonproductive episodes at 50 rads/min, 92 rads/min, and 175 rads/min to be greater than the number of nonproductive episodes at the 12 rads/min rate. These inconsistencies can be attributed to the 2 replicates in each cell of the data matrices (see Table 10). Too many questions were asked with too little data.

#### Comments

Onset and offset times can be measured from three different starting points: when the machine is turned on, when it is turned off, or when some specific dose is delivered regardless of when the machine was turned on or off. When onset is measured from machine-on, a mechanical bias is introduced since lower dose rates take longer to deliver an effective dose of radiation to the subject. In the above data, if the time to deliver 446 rads ( $ED_{50}$  for emesis) is subtracted from all onset and offset times, then onset/offset times would measure the lag time between the delivery of an emetic dose and the time of appearance/disappearance of emesis. If dose rate has a physiological effect on onset/offset times, then these lag times should change at various dose rates.

Subtraction of the time to deliver 446 rads eliminated all evidence of dose rate effects on onset and offset times. For example, onset times measured from machine-on were 107.0 min at 6 rads/min and 48.7 min at 175 rads/min. These are statistically significant differences. Onset times measured from delivery of 446 rads were 32.6 min at 6 rads/min and 46.2 min at 175 rads/min and are not statistically different. This implies that the differences detected in study 31 were mechanical ones due to dose rate, and that the physiologically important event (between 6 rads/min and 175 rads/min) was not dose rate but the accumulation of an effective emetic dose.

Next, we use Type I ( $\alpha$ ) and Type II ( $\beta$ ) errors to discuss the implications of testing 6 dose rates and 2 fasting schedules at once. Recall that a Type I error is the probability of rejecting the null hypothesis when it is true. For this data set, a Type I error is committed when we find either significant dose rate or fasting effects when there should be none. A Type II error is committed when one accepts the null hypothesis when it is false. For this data set, a Type II error is committed when one finds neither significant dose rate nor fasting effects when there should have been some. We believe this may be the case in the present situation.

An alternative to measuring Type II errors is to examine the power of the test where power is  $1-\beta$ . In hypothesis testing the investigator specifies the  $\alpha$ -level he can tolerate and then chooses the sample size to maximize the power of his test. In this way one minimizes the probability of committing a Type II error. Figures 3-5, respectively, show power curves for testing:

- a. Both the hypothesis of no dose rate effect among 6 dose rates and the hypothesis of no fasting effect among 2 fasting schedules.
- b. The hypothesis of no fasting effect among 2 fasting schedules.
- c. The hypothesis of no dose rate effect among 6 dose rates.

Delta ( $\Delta$ ) is the maximum difference between dose rates or fasting schedules that the investigator may wish to detect. Sigma ( $\sigma$ ) is the estimated standard deviation for each variable. Such estimates (the  $\sqrt{\text{MSE}}$  from the ANOVA's) are summarized in Table 11.

To illustrate the use of Figures 3-5, suppose an investigator wishes to detect 30-min onset time differences in dose rates and fasting schedules at the 5% level of significance. In such a case  $\Delta/\sigma = 30/22.99$  or 1.3. From Figure 3 we see that the probability of a correct decision (the power) is 10% for the experiment as it was implemented with 24 subjects. By increasing the sample size by a factor of five to 120 subjects, a more realistic power level of 64% results. If the investigator were willing to omit the question of dose rate effects and concentrate only on the question of fasting effects (with  $\alpha = .05$ ), the same 24 animals would yield a power level in excess of 90% (cf. Fig. 4). On the other hand, if one were willing to use 36 animals to test the hypothesis ( $\alpha = .05$ ) of effects among the 6 dose rates (while sacrificing an answer to the question of fasting effects), the probability of making a correct decision would be 34% (cf. Fig. 5).

Figures 3-5 and the above show that there are a number of ways to increase the probability of making a correct decision. They include:

- a. A decrease in the  $\alpha$ -level (an increase in the Type I error rate).
- b. A decrease in the number of questions asked.
- c. An increase in the maximum difference one wishes to detect.
- d. An increase in the number of animals in each experimental combination.

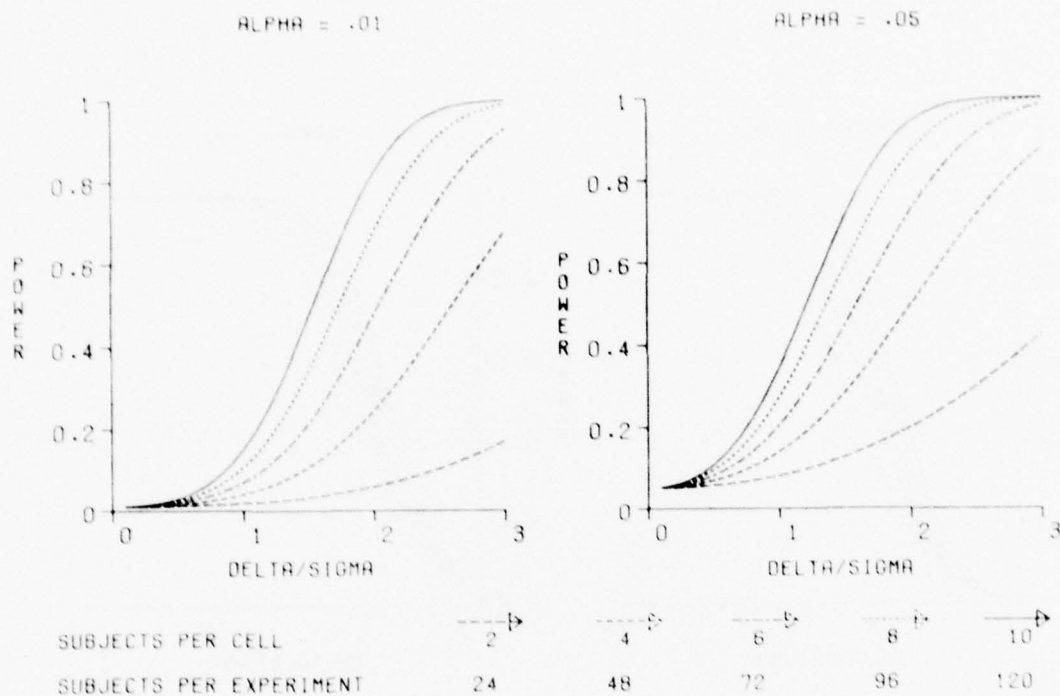


Figure 3. Minimal (worst case) power curves for testing both the hypothesis of no dose rate effect among 6 dose rates and the hypothesis of no fasting effect among 2 fasting schedules.

TABLE 11. ESTIMATES OF  $\sigma$

Variable	Estimates
Onset	22.99 min
Offset	26.45 min
Vulnerability	26.49 min
Total duration	3.50 min
Productive duration	3.12 min
Nonproductive duration	1.74 min
Total No. episodes	1.61 episodes
No. productive episodes	1.26 episodes
No. nonproductive episodes	0.76 episodes

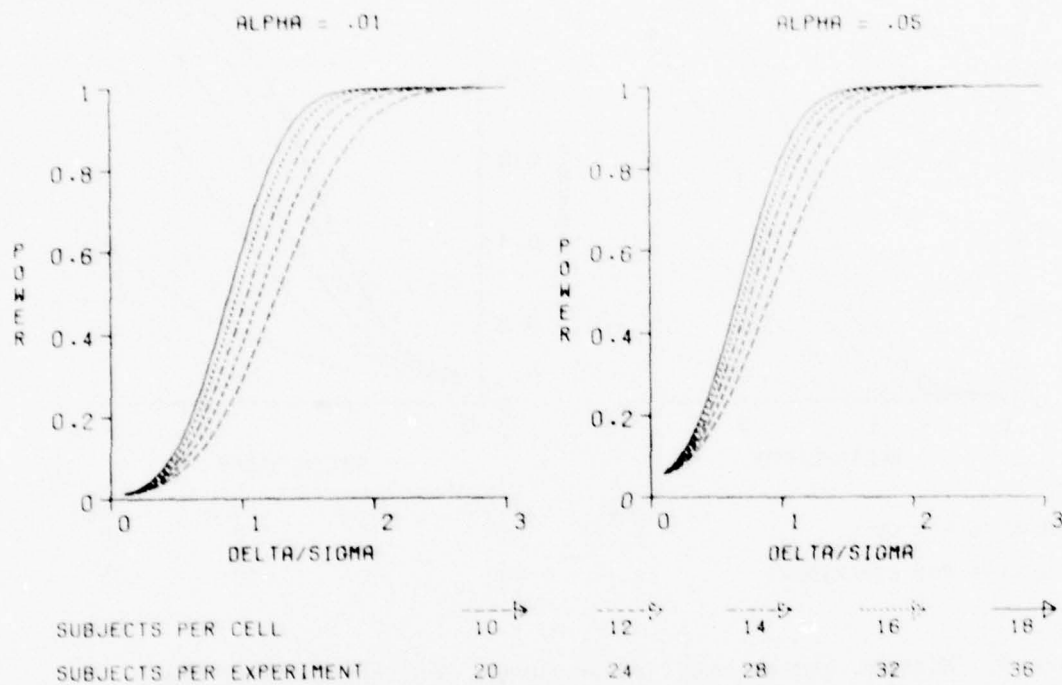


Figure 4. Power curves for testing the hypothesis of no fasting effect among 2 fasting schedules.

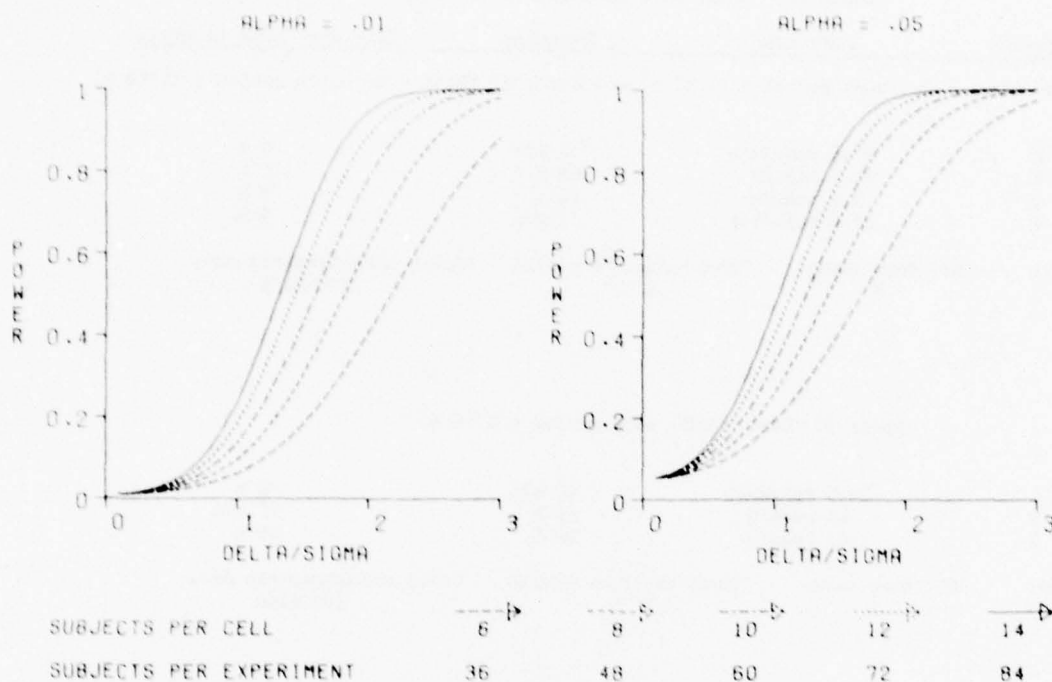


Figure 5. Power curves for testing the hypothesis of no dose rate effect among 6 dose rates.

Accurate estimates of  $\sigma$  are essential to ensure that operationally significant differences can be detected. In the above example 30 min represented a difference of 1.3 standard deviations in onset times. In real-world applications it might turn out that smaller differences in onset times (say 10 min) are relevant differences for detection. This would entail even larger sample sizes. We recommend at least 10 subjects/treatment group for intergroup comparisons.

#### MIXED RATES (Studies 36, 37, 38, 40)

##### Methods

Studies 36, 37, 38, and 40 represent a departure from previous experiments in that they call for scenario-specific profiles. Table 12 summarizes their experimental parameters. All four studies in this section use mixed dose rates protracted over relatively long exposure periods (0-72 h). These studies must be viewed as pilot studies due to their small sample sizes and their unique dose profiles.

TABLE 12. MIXED RATE EXPERIMENTAL PARAMETERS

Sequence	Dose rate	Duration	Time dose rate is given
Study 36 (Task = D-; work period = 11/12 h) and Study 37 (Task = D+; work period = 11/12 h)			
1	27.6 rads/min	2 min	0 h
2	97.8 rads/h	.62 h	1 h
3	9.9 rads/h	10 h	2 h
4	27.6 rads/min	3 min	9 h
Summary:	No. dose rates 4	Total exposure period 12 h	Total midepigasttric dose 302 rads

Study 38 (Task = PEP; work period = 9/72 h)

1	13.5 rads/min	10 min	0 h
2	10 rads/h	10 h	10 min
3	1.05 rads/h	62 h	10 h
Summary:	No. dose rates 3	Total exposure period 72 h	Total midepigasttric dose 300 rads

Study 39 (Task = PEP + MART; work period = 10/10 h)

1	50 rads/min	2 min	0 h
2	17.5 rads/min	2 min	1 h
3	7 rads/min	15 min	2 h
4	1000 rads/min	2 min	7.5 h
Summary:	No. dose rates 4	Total exposure period 10 h	Total midepigasttric dose 1440 rads

Studies 36 and 37 used the same profile to study the effects of both positive (D+) and negative (D-) reinforcement. Animals were trained to perform identical tasks with different rewards and were exposed to identical radiation profiles. One group received food pellets for a correct response. The other group received no food but a shock when they made an incorrect response--negative reinforcement. Table 13 shows the number of animals in each study that had at least one emetic episode.

TABLE 13. EMTIC RESPONSES IN STUDIES 36 AND 37

	Shock Study 36 D-	Food Study 37 D+	Total
Emesis	1	4	5
No emesis	7	3	10
No. of subjects	8	7	15

### Results

Fisher's exact test (cf. 10) found no difference in the proportion of emetic responders between the two studies at the 10% level of significance. This finding is a result of the sample size selected. If no shock animals had vomited, Fisher's exact test would have found a significant difference between studies at the .05 level. Attention must be paid to the questions to be answered and the sample size selected to answer these questions.

It would be nice to compare study 38 with studies 36 and 37 as these studies involved 300-rad total midepigastic doses. However, as enumerated in Table 14, a number of differences between these studies are based solely on selected experimental parameters.

TABLE 14. EXPERIMENTAL PARAMETERS FOR STUDIES 36, 37, AND 38

Studies 36 and 37	Study 38
Discrete avoidance (lever pressing)	PEP
Stationary subjects	Motion
4 different dose rates, durations, and times of administration	3 different dose rates, durations, and times of administration
4 work sessions with 20-minute rest periods between sessions	9 1/2-h work sessions with rest periods of 1/2 h or 4 h between sessions

Even if the sample sizes were sufficiently large to permit valid numerical comparisons between these studies, one would be hard pressed to state the cause of any significant differences detected; should they be attributed to task differences, motion differences, dose-rate differences, or work-rest schedules.

In study 39, subjects were trained to perform two different tasks simultaneously--the continuous PEP (pitch axis only) and the discrete MART. The dose rates differed from the other studies in this section (see Table 12); in addition there were no rest periods. This study differed from other studies throughout the repository in that it is the only 2-task experiment that was implemented. Interstudy comparisons were not possible because of the variety of experimental parameters.

#### Comments

Mixed rate experiments may provide a practical area of research:

- a. Testing for order effects in dose sequences.
- b. Testing for time differences for the same dose sequence.
- c. Testing for time differences for dose rate sequences.
- d. Testing for task differences for the same dose profile.

Each of these areas can be systematically examined and thus provides a foundation upon which general statements can be made. The alternative is to continue looking at scenario-specific profiles which can only answer what might happen under a given set of conditions. Such an approach provides little or no information to field commanders, if the reality of their situation does not closely resemble the experimental scenario reported.

#### DESCRIPTIVE (Studies 3.1, 3.2, 26, 28, 32, 34, 35)

This section contains studies from the repository which could not be classified under any of the other headings. Similarly, they are also pilot studies.

Subjects in studies 3.1 and 3.2 were trained to perform the Landolt ring visual acuity task. Table 15 shows subjects in the two studies were exposed to 1 of 2 doses, 1 of 3 fasting schedules, 1 of 2 continued dose rates, and the same n:y ratio. Multiple experimental parameters coupled with small sample sizes preclude the testing of hypotheses of differences between doses, dose-rates, and fasting schedules for this behavioral task and this neutron-gamma ratio.

TABLE 15. EMETIC RESPONSES AND FASTING SCHEDULE (h) IN STUDIES 3.1 AND 3.2

## Study 3.1

Dose (Pulse, n:y = .5)

No. of subjects	600 rads			1000 rads			Total
	1h	3h	16h	1h	3h	16h	
Emesis	1			1		1	3
No emesis	2	1					3
Total	3	1		1		1	6

## Study 3.2

Dose (200 rads/min, n:y = .5)

No. of subjects	600 rads			1000 rads			Total
	1h	3h	16h	1h	3h	16h	
Emesis	1			2		1	4
No emesis	2						2
Total	3			2		1	6

In Study 26 all subjects were on the same fasting schedule (17 h), dose rate (pulse), neutron-gamma ratio (.65), and task (PEP). They can be grouped into 4 dose ranges as shown in Table 16. Biologic variability and small sample sizes lead to a relatively flat dose-response curve. Emesis did not occur at the highest doses (2035 and 2224 rads) tested.

TABLE 16. EMETIC RESPONSES IN STUDY 26

Dose (rads) (Pulse, n:y = .65)

	283-286	612-653	1092-1283	2035-2224	Total
Emesis	2	1	1	0	4
No emesis	1	1	1	2	5
No. of subjects	3	2	2	2	9

Study 28 was similar to study 26 in that the task (PEP), dose rate (pulse), neutron-gamma ratio (.5), and fasting schedule (1 h) were held constant for all subjects. The small sample size spread over many doses prevents definition of a dose-response curve (Table 17). This experiment did serve the purpose of dose ranging, by identifying the occurrence of emesis in the 540- to 1110-rad dose interval.

TABLE 17. EMETIC RESPONSES IN STUDY 28

	DOSE (rads) (Pulse, n:γ = .5)				
	275	540-550	945-970	1010-1110	Total
Emesis	0	3	2	1	6
No emesis	3	0	0	1	4
No. of subjects	3	3	2	2	10

In study 32 all naive animals were subject to the same experimental parameters: fasting = 1 h; n:γ = 1/4; dose rate = pulse; dose range = 950 - 1130 rads. This study is unique in that only 1 of 12 subjects vomited in this relatively high dose range within the 2-h postexposure period.

Study 34 compared 2 doses (500 and 1000 rads) using naive animals exposed to a 5/1 neutron/gamma ratio. As shown in Table 18, the small sample sizes and different fasting schedules precluded the making of any rigid statements except that emesis can occur at either 500 or 1000 rads.

TABLE 18. EMETIC RESPONSES AND FASTING (h) SCHEDULE IN STUDY 34

Dose (Pulse, n:γ = 5.0)							
	<u>470-530 rads</u>			<u>950-1000 rads</u>			
<u>No. of subjects</u>	<u>1h</u>	<u>3h</u>	<u>6h</u>	<u>1h</u>	<u>3h</u>	<u>6h</u>	<u>Total</u>
Emesis	1			1			2
No emesis	3		4	1		2	10
Total	4		4	2		2	12

Study 35 was another dose-ranging experiment involving 3 different doses where subjects were exposed to the same experimental parameters (a constant n:y ratio; a 1-h fasting schedule; and the PEP pitch and roll task). Table 19 summarizes the occurrence of emesis at the various doses. Onset times were earlier, and the average number of episodes were greater for the 1000-rad dose.

TABLE 19. EMETIC RESPONSES IN STUDY 35

	Dose (Pulse, n:y = 1)			
	250 rads	500 rads	1000 rads	Total
Emesis	3	1	4	8
No emesis	1	1	0	2
No. of subjects	4	2	4	10

The data from 10 studies (2, 3, 18, 19, 27, 28, 31, 33, 35, 39) were arbitrarily grouped together to provide a very gross description of the emetic response following radiation (Table 20). The group total was 89 monkeys representing all aspects of experimental variability such as different doses, dose rates, radiation quality (x,y, n:y), fasting times, and tasks. The objective is simply to provide future experimenters with rough statistical estimates to plan resource commitments, hopefully including fewer questions, more monkeys per treatment group, and longer observation periods.

TABLE 20. STATISTICAL SUMMARY OF GROUPED EMESIS DATA<sup>a</sup>

	$\bar{X}$	Range	S.D.
Onset delay (min)	40.4	1 to 106.9 (min)	18.2
Vulnerable period (min) (Syndrome duration)	31.4	.1 to 217 (min)	35.3
Episodes	2.9	1 to 14	2.1
% Productive	72%	38% to 85%	-

<sup>a</sup>1. N=89 responders

2. Studies 2, 3, 18, 19, 27, 28, 31, 33, 35, 39

3. Since some observation periods were only 2 hours, there may be some data truncation.

4. Onset times for studies 31 and 39 were adjusted for low dose rate by subtracting the time necessary to deliver 450 rads (ED<sub>50</sub> emesis).

## COMPUTER PROGRAMS

This section briefly outlines the computer software used in the analysis of this repository. All programming was done in APL. Source listings of appropriate code are given in Appendix B. This section is not an APL tutorial. Its purpose is to indicate by name and function appropriate software tools so that the repository can be maintained.

### Data Sets

Data set EMESIS.D770323 is organized by study as follows:

<u>Description of data</u>	<u>Field</u>	<u>Description of data</u>	<u>Field</u>
Study number	1-5	Animal type	43-48
Month	7-9	Number of males	50-55
Year	11-12	Number of females	57-61
Experimental site	14-18	Restraint used on subject	63-67
Type radiation used	20-24	Emesis data collected	69-74
Neutron/gamma ratio	26-29	Low dose (Midpigastic)	77-80
Task	31-34	High dose (Midpigastic)	83-86
Hours observed	36-37	Mode of dose administered	88-91
Number of animals	40-41		

The function REPOSITORY accesses this data set. It is user oriented and permits the novice to examine the experimental parameters in all studies currently cataloged in the computer repository. This function can produce tables similar to Table 1 as well as subtables of any of the experimental parameters selected. For example, one can obtain a listing of all PEP experiments or all experiments conducted at White Sands Missile Range.

The data set ALL.EMESIS.D770420, organized by subject and study, contains additional experimental parameters on each animal such as fasting schedule and dose rate as well as what happened on exposure day: the number of emetic episodes, onset and duration times, and the classification of episodes as productive or nonproductive. This data is structured as follows:

<u>Description of data</u>	<u>Field</u>	<u>Description of data</u>	<u>Field</u>
Subject ID	1-5	Pulse size (min)	24-26
Study No.	7-10	Dose rate (rads/min)	28-31
Dose (Midpigastic)	12-15	Number of episodes	33-34
Hours fasted	17-20	Onset time (xxx.xxmin)	36-41
Radiation mode	22	Duration time "	43-47
(0 = steady or mixed rates)		Kind of emesis	49
(1 = single pulse)		(1 = productive; 2 = nonprod)	
(2 = double pulse)		No. of contractions	51-53

The pattern starting in column 36 for onset times, duration times, kinds of emesis, and number of contractions repeats itself (starting in column 55) as many times as is necessary until all episodes have been described.

#### Plot Routines

The graphs in Appendix A were created by the function PLOTEME. This function obtains its data from the ALL.EMESIS.D770420 data set. When called, this function will ask the user to define the study he wishes to draw. The function will automatically draw dose profiles for continuous- and single-pulse experiments. The user must write his own software to draw more complicated dose profiles. DRA33, DRA36, DRA37, and DRA38 are such examples for studies 33, 36, 37, and 38, respectively.

The power and the dose rate curves were drawn by the functions SETUPMOD following correct definition of X and Y variables. These APL functions are general in nature and permit the user to draw as many coordinate axes with as many variables as one specifies.

A graphics DIRECTORY has been created which stores all the illustrations created in this technical report. To display any item in the directory one merely needs to type the word DISPLAY followed by the name of the file to be displayed in quotes. This system will save dollars and time in not having to recreate these illustrations for a second time. A second advantage of this system is that it allows graphic overlays so that different studies can be examined simultaneously.

#### Analysis Programs

Analysis programs developed in this report include LILLYEX X, WEIBULL X, ANOVA X, TUKE2, and DSTAT X. These routines are user oriented and will prompt the user for necessary information. LILLYEX X and WEIBULL X, respectively, test to see if data X has exponential or Weibull distributions. ANOVA X is used to perform a two-factor analysis of variance on a three-dimensional data matrix X where the first dimension represents replicates, levels of the B factor are the second dimension, and the levels of the A factor are the third dimension. TUKE2 will take the output of ANOVA X and perform Tukey's multiple comparison procedures on each factor. DSTAT X will compute means, standard deviations, and other descriptive statistics on the data vector X.

Again, we repeat that the purpose of this section and Appendix B is not to serve as a "how to" guide. Their inclusion is to indicate which tools are currently available in support of this repository. There is no substitute for computer terminal experience and a reading of the REW Emetic Repository Log Book to better learn how to use these tools.

## CONCLUSIONS

Data on ionizing radiation emesis, collected from 21 studies involving 210 rhesus monkeys, has been examined. These studies contained a wide variety of experimental parameters prepared by investigators interested in unique situations. The studies were grouped a posteriori on the basis of the analysis permitted by the data collected.

In several studies the distribution of emesis onset times and episode durations could be determined. In these instances, the onset time of each episode had an exponential distribution, and the duration of each episode was either an exponential or Weibull distribution. The presence of similar distributions across many experiments suggests that the same mechanism is at work in each study and episode, differing only in intensity.

One study found the  $ED_{50}$  for radiation emesis to be 446 rads ( $Co^{60}$ , 20 rads/min), and that motion reduced the  $ED_{50}$  to 258 rads. Another study (No. 31) demonstrated 100% incidence of emesis at 550 rads (X-ray, 6 to 175 rads/min).

Although designed to answer other research questions, these studies are good emesis syndrome pilot studies in that they refine experimental techniques, permit the training of personnel and the development of SOPs, and provide experience for contingency plans. They provide the opportunity to operationally define what is to be measured; they facilitate the selection of competing metrics, and suggest how long the measurement process should occur.

The effects of such factors as dose rate, fasting time, radiation quality, and performance tasks on the radiation emesis syndrome are still undetermined. The present studies provide estimates of  $\sigma$  for planning fully developed emesis experiments so understanding of the interrelationships between  $\alpha$ -levels, number of questions to be answered, operationally relevant differences to be detected, and the sample size selected can result in cost-effective experiments with a high payoff in valid findings. As a rule of thumb, we recommend at least 10 subjects per treatment group in making intergroup comparisons.

#### ACKNOWLEDGMENTS

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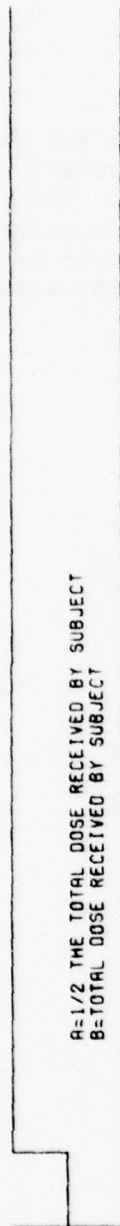
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## APPENDIX A

### PICTORIAL SUMMARY OF EMETIC FINDINGS

Appendix A is a graphical summary of emetic findings for the studies listed in Table 1. Bars 2 units high indicate productive episodes. Bars 1 unit high indicate nonproductive episodes. Width of bars indicate episode duration. Flat lines show no emetic activity between emetic episodes. Absence of bars and lines indicate no emetic signs during the observation period given in Table 1. This appendix is organized by study numbers presented in Table 1.

STUDY DATE 2 MAR 72 SITE TYPE N/Q TASK HRS NO. ANIMAL SEX RESTR EMESIS LOW DOSE HIGH DOSE  
 NO. RAY RAD. 0.72 0- 15 16 RHESUS 1 MALE DOFEM BEHAV EMESIS 2160 2650 2PUL  
 TIME IN MINUTES 0 20 40 60 80 100 120 140 160 180



10 DOSE HRFD  
 28 2160 17.0  
 34 2190 17.0  
 24 2410 17.0  
 36 2430 17.0  
 32 2490 17.0  
 22 2520 17.0  
 23 2520 17.0  
 26 2530 17.0  
 33 2530 17.0  
 27 2580 17.0  
 35 2590 17.0  
 25 2600 17.0  
 21 2620 17.0  
 30 2620 17.0  
 31 2630 17.0  
 29 2650 17.0

STUDY NO.	DATE	SITE	TYPE	N/G	TASK	HRS	NO.	ANIMAL	SEX	RESTR	EMESIS	LOW DOSE	HIGH DOSE	MODE	
3.1	OCT 71	A-M	N/G	0.5	LAND	2	6	Rhesus	Female	DOFEM	BEHAV	EMESIS	600	1000	IPUL

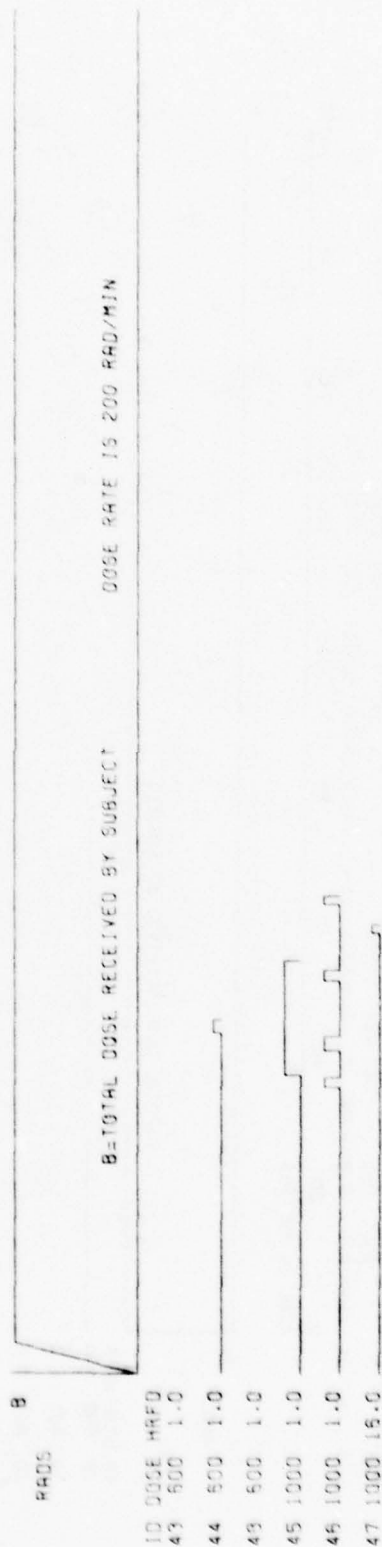
TIME IN MINUTES



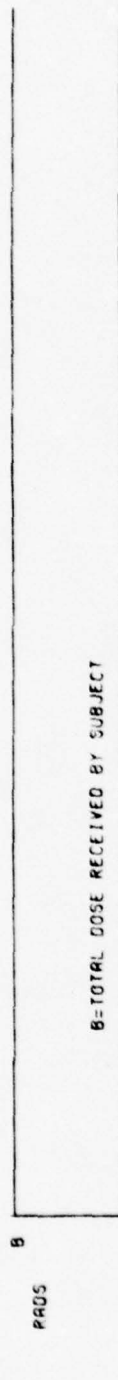
ID	DOSE	HRFD
38	600	1.0
39	500	1.0
40	500	1.0
49	500	3.0
41	1000	15.0
42	1000	1.0

B=TOTAL DOSE RECEIVED BY SUBJECT

STUDY NO.	DATE	SITE	TYPE	N/G	RAD.	TASK	HRC	NO.	ANIMAL	SEX	REGIR	EMESIS	LOW	HIGH	MODE
3-2	OCT 71	A-M	N/G	0.5	LAND	2	5	RHECUS	5MALE	DOFEM	BEHAV	EMESIS	500	1000	SIED

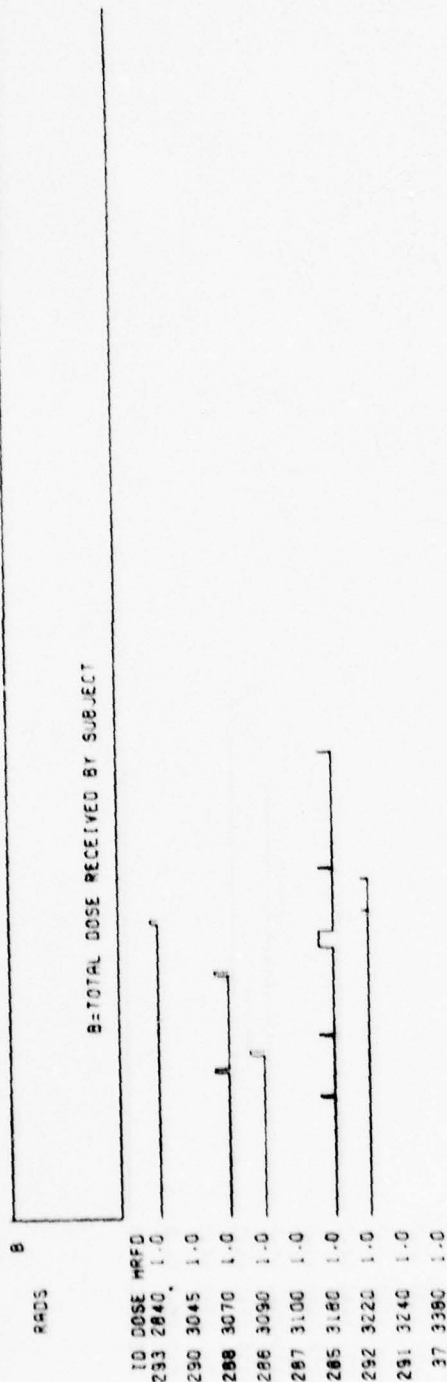


STUDY DATE SITE TYPE N/C TASK MRS NO: ANIMAL SEX RESTR EMESIS LOW HIGH MODE  
 NO. 18 JUL 71 AFRI N/C 0.24 PEP 22 11 RHESUS 11MALE 00FEM BEHAV EMESIS 1020 2920 1PUL  
 TIME IN MINUTES 0 20 40 60 80 100 120 140 160 180

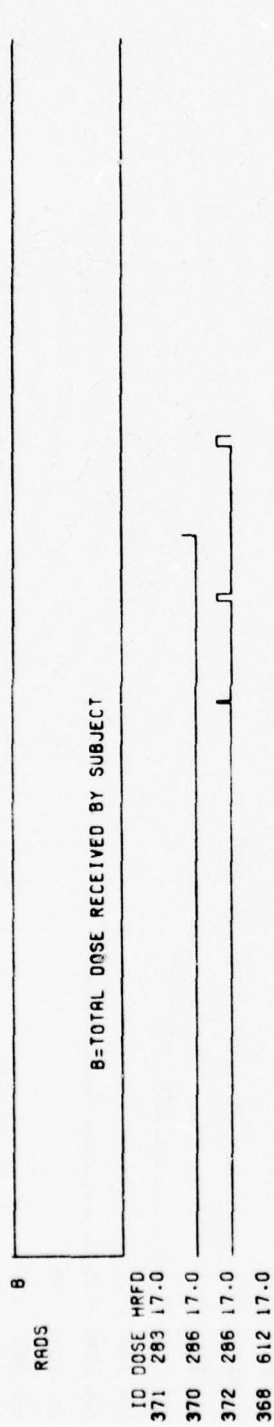


ID DOSE HRFD  
 284 1020 1.0  
 283 1050 1.0  
 281 1080 1.0  
 282 1130 1.0  
 277 2440 14.0  
 278 2580 14.0  
 273 2600 14.0  
 275 2740 14.0  
 276 2780 14.0  
 279 2890 14.0  
 280 2920 14.0

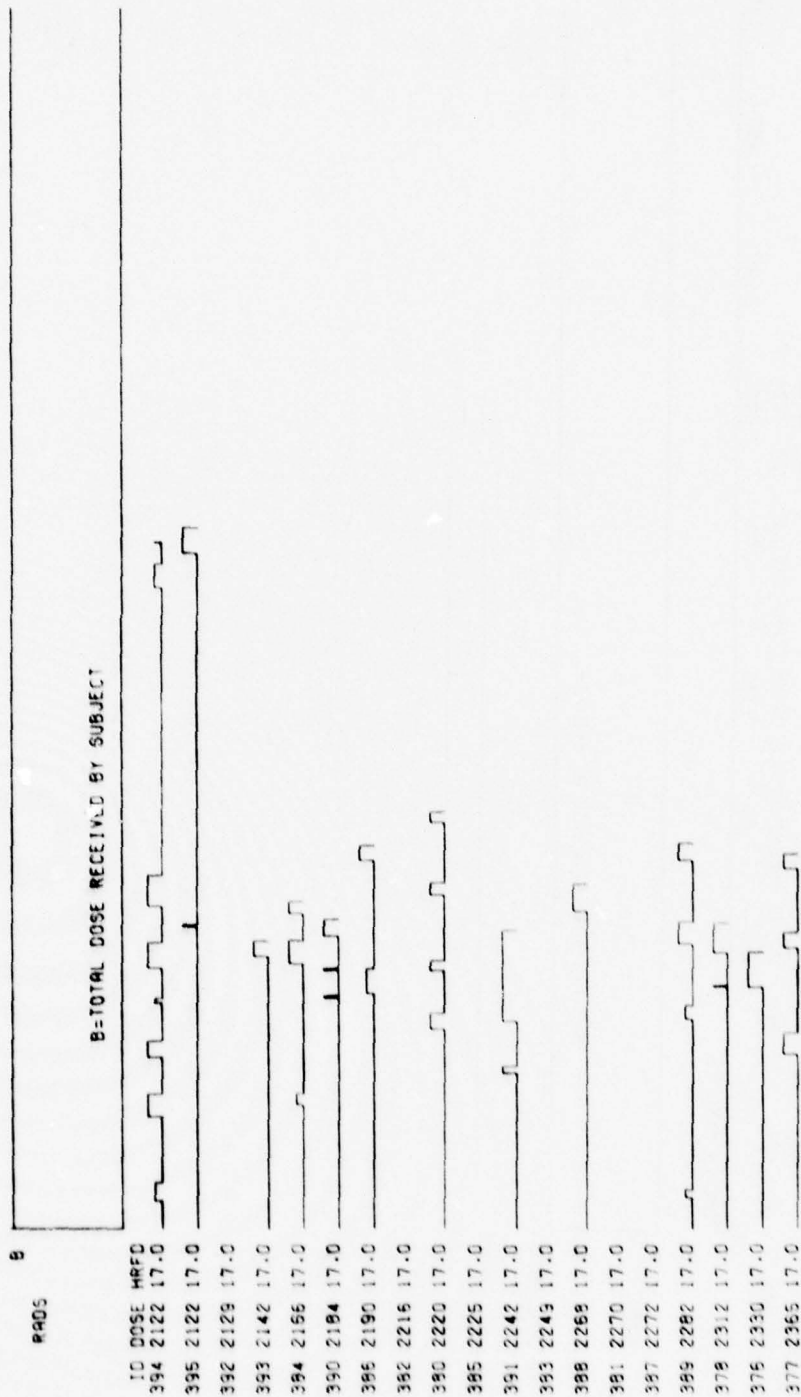
STUDY DATE 15 MAR 72 SITE TYPE A-M N/G RAY N/G TASK HRS NO: ANIMAL SEX RSTR EMESIS LOW DOSE HIGH DOSE  
 NO. 22 09 RHESUS 03MALE DOFEM BEHAV EMESIS 2840 3380 1PUL  
 TIME IN MINUTES 0 20 40 60 80 100 120 140 160 180



STUDY DATE SITE TYPE N/G TASK HRS NO. ANIMAL SEX RESTR EMESIS LOW HIGH MODE  
 NO. 26 AUG 72 A-M N/G 0.65 PEP 2 09 RHESUS 09MALE 00FEM BEHAV EMESIS 283 2224 1PUL  
 TIME IN MINUTES



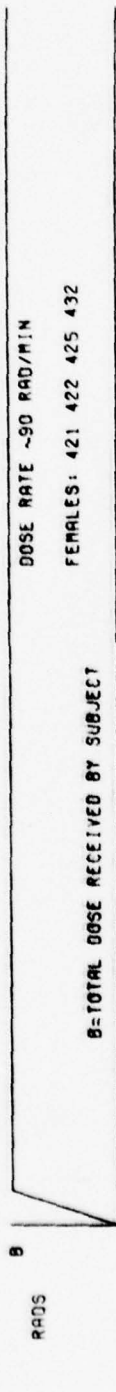
STUDY DATE 27 AUG 72 SITE TYPE N/G TASK HRS NO. ANIMAL SEX RESTR EMESIS LOW DOSE HIGH DOSE  
 NO. 27 AUG 72 A-M N/G 0.44 D- 2 19 RHESUS 19MALE DOFEM BEHAV EMESIS 2122 2366 IFUL  
 TIME IN MINUTES 0 20 40 60 80 100 120 140 160 180



STUDY DATE SITE TYPE N/G TASK HSG NO. ANIMAL SEX RESTA EMESIS DOSE HIGH DOSE  
 NO. 29 MAR 73 R-M N/G C-5 PEP 2 10 RHESUS 10MALE 00FEM BEHAV EMESIS 170 1110 1PUL

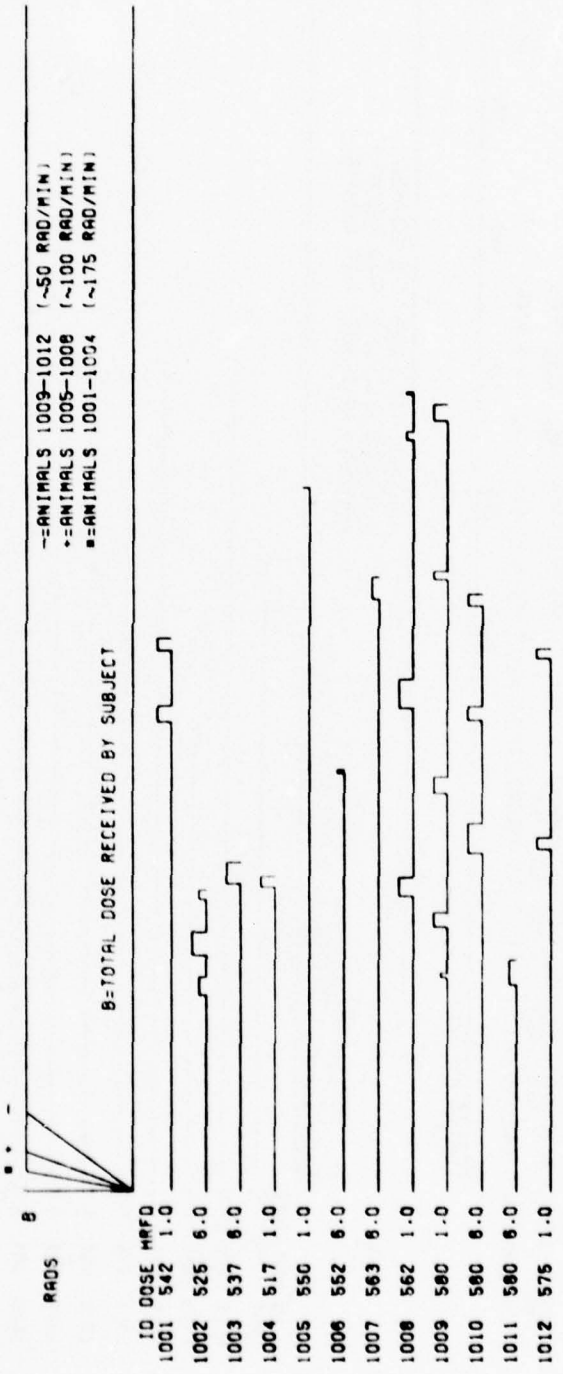


STUDY DATE 30 OCT 73 SITE TYPE N/C TASK HRS NO. ANIMAL SEX RESTR EMESIS LOW DOSE HIGH MODE  
 NO. 005 RAY 0- 2 12 RHESUS 08MALE 04FEM PHYSI EMESIS 341 520 STED  
 SAM X-RAY 0 20 40 60 80 100 120 140 160 180  
 TIME IN MINUTES



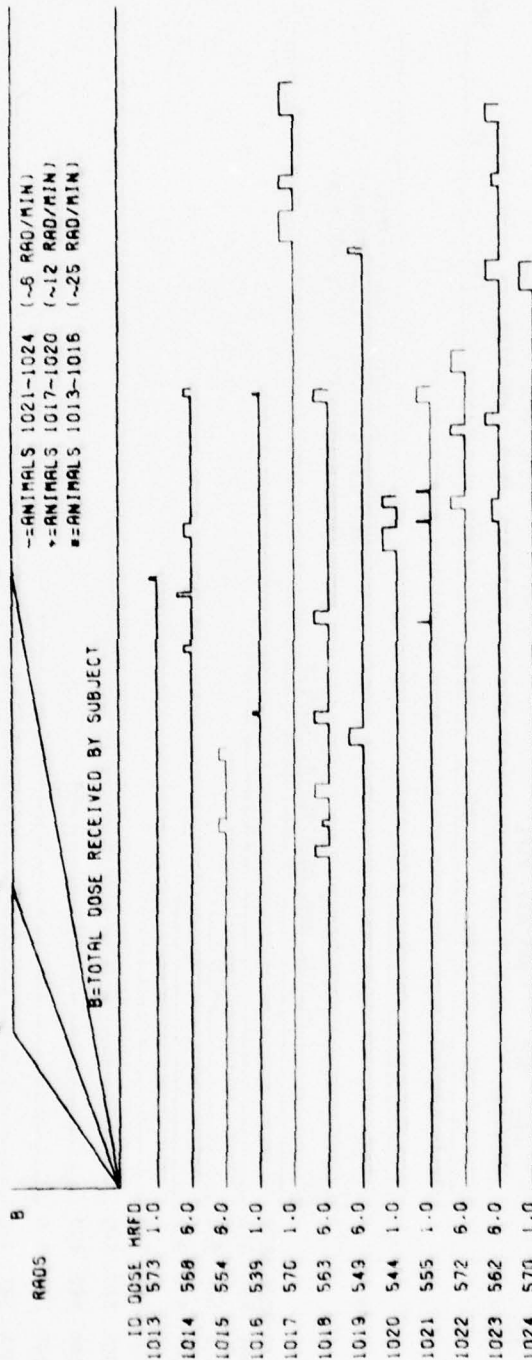
ID	DOSE	HREF
428	341	.0
425	513	.0
423	515	.0
429	515	.0
430	515	.0
422	516	.0
432	516	.0
421	523	.0
427	523	.0
424	525	.0
426	525	.0
431	528	.0

STUDY DATE 31.1 MAY 71 SITE TYPE N/A TASK HRS NO. ANIMAL SEX RESTR EMESIS LOW HIGH MODE  
 NO. 31.1 MAY 71 RAD: RAY OBS ANS TYPE MAIV 2 12 RHESUS 12MALE DOFEM NATVE EMESIS 5.7 580 STED  
 SAM X-RAY TIME IN MINUTES 0 20 40 60 80 100 120 140 160 180

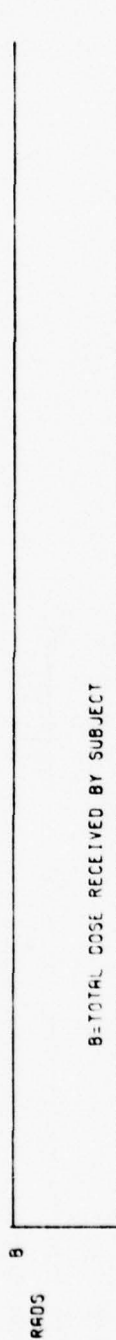


STUDY DATE 31.2 MAY 71 SITE TYPE N/G TASK HRS NO: ANIMAL SEX RESTR EMESIS LOW HIGH MODE  
 NO. 31.2 MAY 71 RAD. RA NAIV 2 12 RHESUS 12MALE DOFEM NAIVE EMESIS 539 573 STED  
 SAM X-RAY

TIME IN MINUTES 0 20 40 60 80 100 120 140 160 180

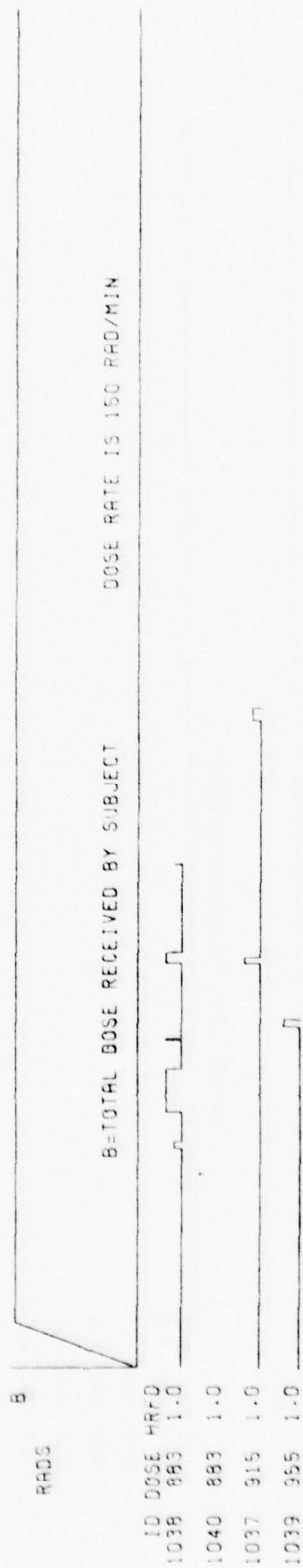


STUDY DATE SITE TYPE N/G TASK HRS NO: ANIMAL  
 NO. 32 JUL 71 AFRI N/G 0.24 NAIV 2 12 RHESUS 12MALE DOFEM BEHAV EMESIS 950 1130 1PUL  
 TIME IN MINUTES



IC DOSE HRFD  
 1031 950 1.0  
 1035 960 1.0  
 1030 970 1.0  
 1034 970 1.0  
 1032 980 1.0  
 1029 990 1.0  
 1027 1000 1.0  
 1033 1000 1.0  
 1036 1000 1.0  
 1028 1080 1.0  
 1025 1100 1.0  
 1026 1130 1.0

STUDY DATE 33 SEP 71 SITE TYPE N/C TASK HRS NO. ANIMAL SEX RESTR EMESIS LOW HIGH MODE  
 NO. 33 SEP 71 RAD: RAY OBS 2 04 RHESUS 04MALE 00FEM 5EHAV EMESIS 883 955 STED  
 SAM X-RAY TIME IN MINUTES 0 20 40 60 80 100 120 140 160 180



B=TOTAL DOSE RECEIVED BY SUBJECT

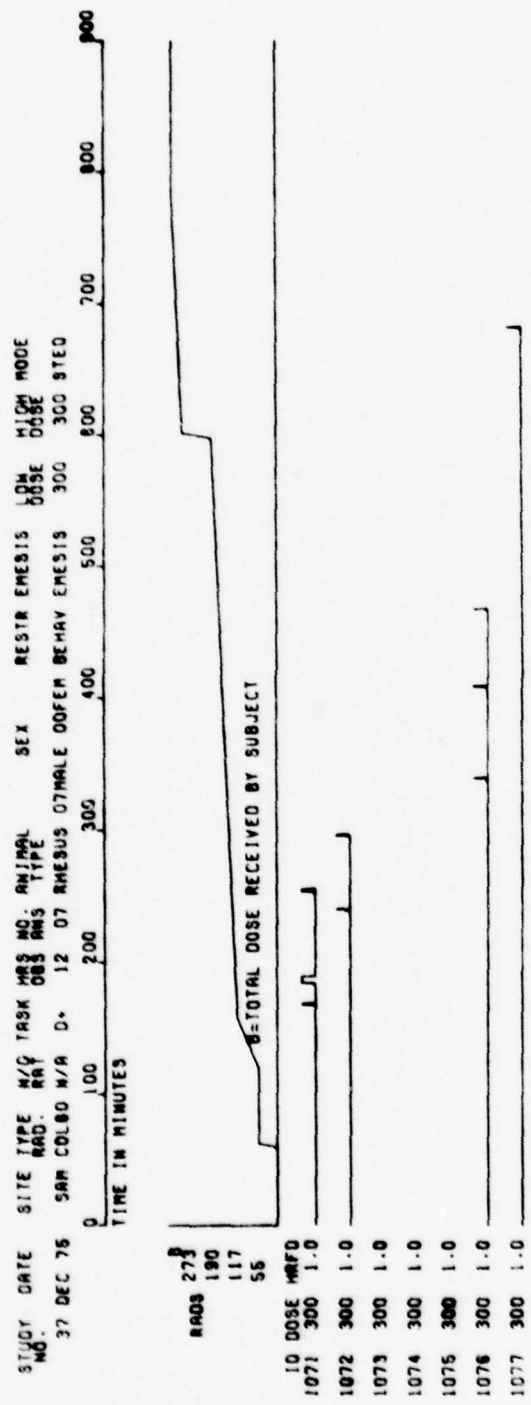
8=TOTAL DOSE RECEIVED BY SUBJECT

ID	DOSE	WFOF
1043	470	1.0
1046	470	6.0
1044	480	1.0
1045	480	6.0
1041	490	1.0
1042	490	1.0
1047	510	6.0
1048	530	6.0
1049	950	1.0
1050	970	1.0
1052	980	6.0
1051	1000	6.0

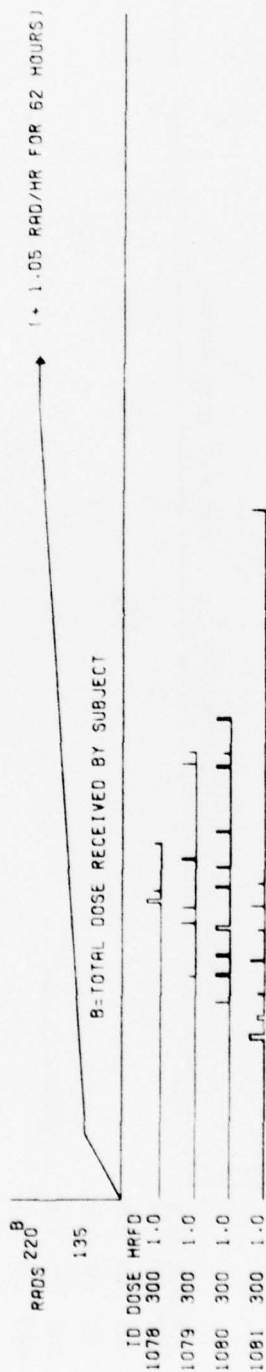


B	
RADS	273
	190
	117
	55
D=TOTAL DOSE RECEIVED BY SUBJECT	
10 DOSE HRFD	
1063	300 1.0
1064	300 1.0
1065	300 1.0

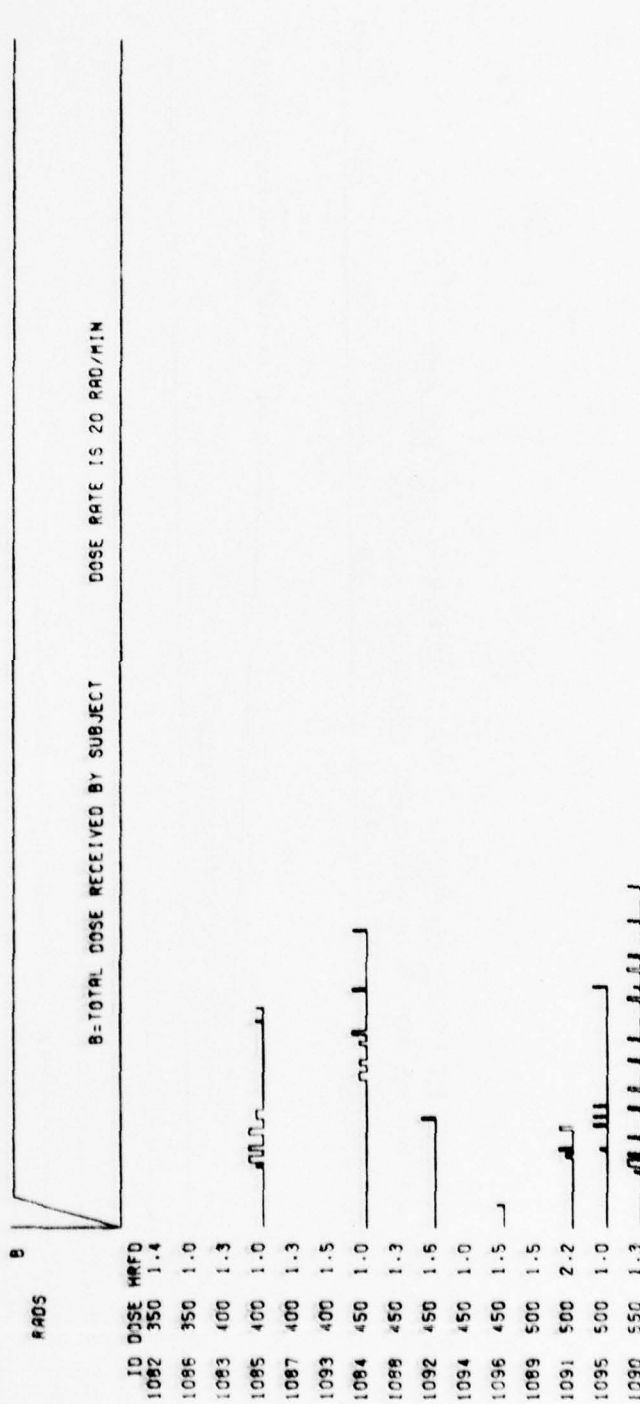
ID	DOSE	HRFD
1063	300	1.0
1064	300	1.0
1065	300	1.0
1066	300	1.0
1067	300	1.0
1068	300	1.0
1069	300	1.0
1070	300	1.0



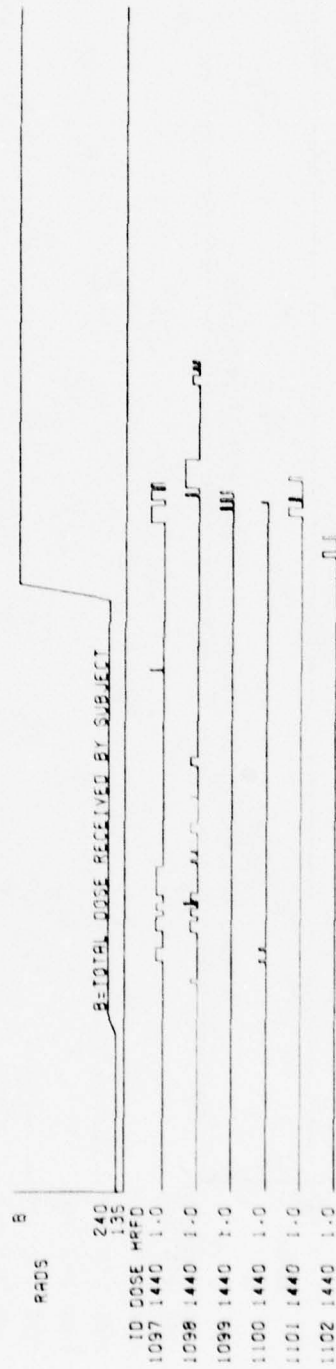
STUDY DATE SITE TYPE N/Q TASK HRS NO. ANIMAL SEX RESTR EMESIS LOW HIGH MODE  
 NO. 38 DEC 76 SAM COL60 N/A PEP 72 04 RHESUS 04MALE 00FEM 00BEH 300 300 300 STED  
 TIME IN MINUTES



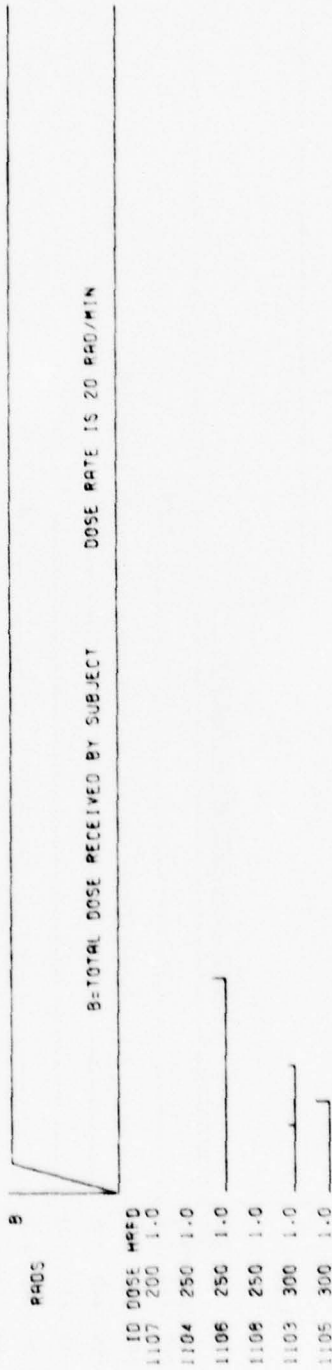
STUDY DATE 39 MAR 77 SITE TYPE N/Q TASK MRS NO: ANIMAL SEX MESTR EMESIS LOW DOSE HIGH DOSE  
 NO. 39 MAR 77 SAM COL60 M/A NAIV 4 IS RHESUS 15 MALE 00FEM CHAIR EMESIS 350 550 STED  
 TIME IN MINUTES



STUDY DATE SITE TYPE N/O TASK HRS NO ANIMAL SEX RESTR EMESIS LOW HIGH MODE  
 40 DEC 76 SAM COL60 N/A PHAR 10 6 RHESUS DEMALE DOFEM BEHAV EMESIS 1440 1440 STED  
 0 100 200 300 400 500 600 700 800 900  
 TIME IN MINUTES



STUDY DATE 41 APR 77 SITE TYPE SAM COL 60 N/A TASK N/A OBS NO. 4 SEX MALE DOSE RATE 20 RAD/MIN  
 NO. 41 APR 77 SAM COL 60 N/A TASK N/A OBS NO. 4 SEX MALE DOSE RATE 20 RAD/MIN  
 0 100 200 300 400 500 600 700 800 900  
 TIME IN MINUTES



## APPENDIX B

### COMPUTER SOURCE CODES

Appendix B is a listing of computer source codes from which the present repository analysis and maintenance was possible. The major functions include:

REPOSITORY  
PLOTME  
SETUPMOD  
DIRECTORY  
LILLYEX X  
WEIBULL X  
ANOVA X  
TUCE2  
DSTAT X

Appropriate subroutines are also listed. The inclusion of this appendix is to identify computer tools presently in support of this repository. It is not a "how to" guide.

```

VREPOSITORY[ ]
V REPOSITORY:QIO:DATA;LP;R:KEY;T:I;NR
[1] 'THIS PROGRAM WILL ALLOW THE USER TO DIVIDE THE SUMMARY TABLE OF STUDIES BY THE ASPECTS OF THE STUDIES'
[2] 'PLEASE WAIT WHILE FILE IS BEING LOCATED'
[3] QIO+1
[4] DATA+LOADMEKIS
[5] LP+1+oDATA
[6] -('YES' ASK 'DO YOU WANT TO SEE A SUMMARY TABLE OF THE STUDIES?')/YES
[7] -L2
[8] YES:RHEADER
[9] DATA
[10] L2+('YES' ASK 'DO YOU NEED AN EXPLANATION OF HOW TO SUBDIVIDE THE SUMMARY TABLE?')/YESA
[11] -NOA
[12] YESA:TEX 3
[13] 'YOU WILL BE ASKED IF YOU WANT TO SUBDIVIDE THE SUMMARY TABLE. IF YOU ANSWER NO THE PROGRAM WILL TERMINATE.'
[14] 'IF YOU ANSWER YES YOU WILL BE ASKED TO TYPE IN A KEYWORD FROM THE TABLE OF ABBREVIATIONS.'
[15] 'YOU CAN CONTINUE THIS PROCESS UNTIL YOU NO LONGER WANT TO SUBDIVIDE.'
[16] 'THE ABBREVIATION TABLE FOLLOWS:'
[17] ' '
[18] DO
[19] NGA: ' '
[20] RESTART:R-(Q,LP)P ' '
[21] -('YES' ASK 'DO YOU WANT TO SUBDIVIDE THE SUMMARY TABLE?')/YESB
[22] -NOB
[23] YESB:KEY+1 ASK 'TYPE IN THE KEYWORD YOU WANT THE TABLE TO BE SUBDIVIDED BY'
[24] I+Q
[25] NR+1+oDATA
[26] LP+('NR<I+1')/OUT
[27] -('O=DATA[I;] PATTERN KEY')/LP
[28] P+R[1] DATA[I;]
[29] -L2P
[30] OUT+('YES' ASK 'DO YOU WANT TO SUBDIVIDE THE NEW TABLE AGAIN?')/YESC
[31] -NOC

```

```

VREFOSITORF[32]V
[32] YESC:TYPE IN THE KEYWORD THAT YOU WANT TO SUBDIVIDE BY'
[33] KEY=I
[34] I=0
[35] T=(0,LR)p'
[36] NR=I+PR
[37] LP2:=(NR-I+1)/OUT2
[38] -(0=PR[;]) PATTERN KEY)/LP2
[39] T=T,[1] R[;]
[40] +LP2
[41] OUT2:R+T
[42] -OUT
[43] NOC:TEX 3
[44] PHEADER
[45] R
[46] ' '
[47] NOB:-( 'YES' ASK 'DO YOU WANT TO GO THROUGH THIS PROCESS AGAIN USING DIFFERENT KEYWORDS?' )/RESTART

VLOADENESIS[1]V
P-LOADENESIS[1]C,SHR1;LR:L,I
[1] DIC+1
[2] I+EX 'SHR1'
[3] ' ' CHX 'SHR1' TRY 'SR DSN=EB.43801.2652007.ENESIS.DT70=20,DISP=SHR,UNIT=3330,VOL=000062,CODE=A'
[4] DIC+1
[5] LR+0
[6] LP:L-SHR1
[7] -(0=PL)/END
[8] -(0=LR)/GO
[9] LP+PL
[10] P-(0,LR)p'
[11] GO:R-R,[1] L
[12] -LP
[13] END:I-EX 'SHR1'

```

```

VASK[0]V
  V R-ANS ASK TEXT:NA,NT
  NT=1+TEXT
  [1] LP:R-NT+0,00-TEXT,
  [2] -(0=PR)/LP
  [3] -(0=NA+0ANS)/0
  [4] R-ANSA,=NA+R
  [5]
  V
VDD[0]V
  DD
  [1] ABBREVIATION
  [2] USEAGE
  [3] MEANING
  [4]
  [5]
  [6]
  [7]
  [8]
  [9]
  [10]
  [11]
  [12]
  [13]
  [14]
  [15]
  [16]
  [17]
  [18]
  [19]
  [20]

```

ABBREVIATION	USEAGE	MEANING
'EYESIS	EYESIS	COLLECTED EYESIS DATA
'A-M	LOCATION	TEXAS A-M UNIVERSITY
'AFERI	LOCATION	ARMED FORCES RAD. RESEARCH INSTITUTE
'NSL	LOCATION	NORTHROP SPACE LABORATORIES
'SAN	LOCATION	SCHOOL OF AEROSPACE MED.
'TRES	LOCATION	TRANSIENT RAD. EFFECTS
'SNE	LOCATION	WHITE SANDS MISSILE RANGE
'UNRES	RESTRAINT	UNRESTRAINED
'BEHAV	RESTRAINT	BEHAVIORAL CHAIR
'PHYSI	RESTRAINT	PHYSIOLOGICAL RECORDING CHAIR
'W/G	RADIATION	MIXED NEUTRON/GAMMA
'X-RAY	RADIATION	LINAC X-RAY
'NEUT	RADIATION	NEUTRON PIPE
'FLASH	RADIATION	FLASH X-RAY
'COB60	RADIATION	COBALT 60 GAMMA



```

VPLOTME[[]]
? PLOTME;ST;IO;N
[1]  IO←1
[2]  USING CENTIMETERS,4015,FOCUS,BUFFERED
[3]  SET CHARSIZE TO 3
[4]  SET SCALE TO 0.18 0.18
[5]  ANMODE
[6]  ERASE
[7]  EMEINP
[8]  OLP;THE VARIABLE AVAILABLE FOR COMPARISON OPERATIONS IS "STUDY"
[9]  COMPO←" ASK 'ENTER THE COMPARISON OPERATION '
[10] INDX←((8*COMPO)/16*STUDY)-1
[11] J←1
[12]  ←(0=INDX)/NOGO
[13]  ERASE
[14]  HEAD
[15]  PL← 0.20
[16]  STRING 'TIME IN MINUTES' AT 5 25
[17]  STRING ' ID DOSE HRFD' AT 0 20.5
[18]  MOVE TO 5 25.5
[19]  I←0
[20]  SCAL←1
[21]  ←(36>8*(6+COMPO))/SCL
[22]  SCL2
[23]  SCAL←15
[24]  ←RDLP
[25]  SCL:SV←SVSTAT
[26]  DRAW 0 1
[27]  MOVE 0 0.5
[28]  STRINGV
[29]  RESTAT SV
[30]  ←(180<I-I+20)/RDLP

```

```

[31] VELOCITE([31])V
[32] DRAW 20 0
[33] -S2L
[34] RDP:RECEIVE INDX
[35] -('DOSE'*.M+COMPO)/LP
[36] DRDOS
[37] LP:ONS+PDONG
[38] -(*D=ONG)/CO
[39] STRING(5 0 MID,DOS),(5 1 VERR) AT PL
[40] PL[1]+PL[1]+5
[41] MOVE TO PL
[42] M+1+ONG
[43] I+0
[44] DP+0
[45] ILP:-(N+I+1)/OUT
[46] DP+ONS[I;1]-DP
[47] PROD
[48] DP+ONS[I;1 2]
[49] -ILP
[50] OUT:PL+0,PL[2]-0.9
[51] -LP
[52] GO:MOVE TO PL
[53] ANYMODE
[54] -('NO' ASK 'HARD COPY ?')/CO1
[55] HECOPY 1
[56] ' '
[57] -CO1
[58] NOCO: NO DATA CONFORMS TO YOUR SPECIFICATIONS'
[59] CO1:-(('NO' ASK 'CONTINUE ?'))/END
[60] ERASE
[61] -OLP
[62] END:ENDIOPLT

```

```

VEMENP[0]
V ENEINF: A
[1] A+CEX 2 4 P'PTR BUFF'
[2] BUFF+10
[3] ' ' CEX(2 4 P'PTR BUFF') TRY 'IR DSN=HB.438C1.2652007.ALL.EMESIS.D770420.DIEP=OLD.CODEZ=A'

V HEAD[0]
[1] HEAD: I: N: COME: DIO
[2] DIO+1
[3] USING DIRECT
[4] ' ' STUDY: A: *6: COMPO: /END
[5] COME+6+COMPO
[6] N+1+SUMMARY
[7] I+0
[8] LP: (N-I+1)/END
[9] ' ' SUMMARY: I: 15: V: *95+COMO: /LP
[10] STRING(HEADER(1:)) AT 1 27.5
[11] STRING(HEADER(2:)) AT 1 27.1
[12] ' ' STRING(SUMMARY(1:)) AT 1 26.5
[13] END: STRING COMPO AT 1 27.5

V PDEME[0]
V PDEME INDX: DIO
[1] DIO+1
[2] S+ 0 319 0 ' '
[3] LP: (0=0: INDX)/END
[4] PTR+0.1+INDX
[5] ' ' CHK PTR
[6] INDX+1+INDX
[7] S+S: [1] BUFF
[8] P+S[1:22]
[9] P8+S[1: 24 25 26]
[10] -LP

V PDEME[0]
[1] END: STU+31.1: 7 8 9 10]
[2] ' ' (STU+31.1) * (STU+31.2) / SORTST
[3] BUFF+ 12 13 14 15 CSORT S
[4] +0
[5] SORTST: BUFF+ 2 3 4 5 CSORT S

V PDEME[0]
V P+PDONS: DIO
[1] DIO+1
[2] R+10
[3] ' ' (J+1+BUFF)/0
[4] P+BUFF[J:]
[5] J+J-1
[6] J+J-1+14
[7] DOS+J+P[11+14]
[8] HRP+0
[9] ' ' (R[16+14])/NOST
[10] HRP+R[16+14]
[11] NOST: (A/ 'R+35+P)/END
[12] ' ' (R[10]= ' ' ) * (R[18]= ' ' ) /OK
[13] R[18]+0
[14] OK: R+((OPR)+4), 4) OPR+R
[15] +0
[16] END: R+ 0 4 0 0

V

```

```

VCSORT([[]]V
  R←N CSORT D
  [1] →(0≤cN)/LIC+2
  [2] →LIC+2
  [3] N←1+D
  [4] D←D(A(' ,DAV)\,D[:1+N]:]
  [5] N←1+N
  [6] →(0≤cN)/LIC-2
  [7] R←D
  V

```

```

VEROD([[]]V
  PROD
  [1] →(ONSLI:3)=1)/DRA1
  [2] DRAW(DP×SCAL),0,0,1,(ONSLI:2)×SCAL,0,0,1
  [3] →0
  [4] DRA1: DRAW(DP×SCAL),0,0,2,(ONSLI:2)×SCAL,0,0,2
  V

```

```

VDRDOS[ ]?
  DRDQ
  I=0
  [1] MOVE TO 5 21
  [2] SV-SVSTAT
  [3] DRAW 0 16
  [4] RESTAT SV
  [5] DRAW 180 0
  [6] RESTAT SV
  [7] + (P=1)/OU
  [8] + (P=0)/LF
  [9] CONTROL(',-COMPO)/COMPO]+ '0'
  [10] 8('DRA',(8+COMPO))
  [11] +STR
  [12] IF:-(P=I+1)/LP1
  [13] DRAW 0,(15.57*1+P),(PS),0
  [14] +LP
  [15] LP1: DRAW 0,(15.57*1+P),(180-PS+1 1),0
  [16] STRING 'A' AT 4.2 22.25
  [17] STRING 'A=1/2 THE TOTAL DOSE RECEIVED BY SUBJECT' AT 10 22
  [18] +STR
  [19] OU: DRAW 0 15.57 180 0
  [20] STR: STRING 'B' AT 4.2 23.57
  [21] STRING 'B=TOTAL DOSE RECEIVED BY SUBJECT' AT 10 21.5
  [22] STRING 'RADS' AT 2 23
  [23]

```

```

VSC2[ ]?
  SCL2
  [1] SCL: SV-SVSTAT
  [2] DRAW 0 1
  [3] MOVE 0 0.5
  [4] STRING I
  [5] RESTAT SV
  [6] + (900<I+100)/0
  [7] DRAW 20 0
  [8] +SCL
  [9]

```

```

VENDIOPLET[ ]V
V ENDIOPLET:A
[1] A+CEX 2 4 0 PTR BUFF'
V
V DRA38[ ]V
[1] DRAW 10 5.3 110 7 8 0 1 0.7 0 1.4 1 0.7
[2] STRING '(+ 1.05 RAD/HR FOR 62 HOURS)' AT 27.94 23.21
[3] STRING '220' AT 3.39 23.21
[4] STRING '135' AT 3.39 21.92
V
V DRA33[ ]V
[1] DRAW 6 15.57 174 0
[2] STRING 'DOSE RATE IS 150 RAD/MIN' AT 23.59 21.5
V

```

```

V DRA36[ ]V
[1] DRAW 12 0 0.4 2.75 11.6 0 7.6 3.1 88 3.65 0.6 4.15 36 1.5 23.8 0
[2] STRING '55' AT 3.5 21.4
[3] STRING '117' AT 3.5 22
[4] STRING '190' AT 3.5 22.6
[5] STRING '273' AT 3.5 23.2
V

```

```

V DRA37[ ]V
[1] DRAW 12 0 0.4 2.75 11.6 0 7.6 3.1 88 3.65 0.6 4.15 36 1.5 23.8 0
[2] STRING '55' AT 3.5 21.4
[3] STRING '117' AT 3.5 22
[4] STRING '190' AT 3.5 22.6
[5] STRING '273' AT 3.5 23.2
V

```

```

VSETUPMOD[ ]V
  SETUPMOD[ ]IO;NPLOTS:S;C:XL:YL:DATA
  [ ]IO←1
  [1] ANMODE
  [2] SET CHARSIZE TO 3
  [3] NPLOTS←1 ASK 'ENTER NUMBER OF PLOTS:'
  [4] YLIMIT←S+C-10
  [5] XL←YL-0 20 p10
  [6] DATA←0 80 p1-0
  [7] LOOP←(NPLOTS<I+1)/OUT
  [8] 'PLOT 'I
  [9] C←C,80 ASK 'ENTER ORIGIN LOCATION IN INCHES:'
  [10] S←S,80 ASK 'ENTER AXES LENGTHS IN INCHES:'
  [11] YLIMIT←YLIMIT,80 ASK 'ENTER Y LIMITS'
  [12] XL←XL,[1] 20 ASK 'ENTER X-AXIS LABEL'
  [13] YL←YL,[1] 20 ASK 'ENTER Y-AXIS LABEL'
  [14] DATA←DATA,[1] 80 ASK 'ENTER DATA SET TO BE PLOTTED:'
  [15] →LOOP
  [16] OUT:II←0
  [17] TEK 2
  [18] USING SCREEN
  [19] SET ROTATION TO 0
  [20] C←(C2,(OC)+2)OC
  [21] S←(S2,(OS)+2)OS
  [22] YLIMIT←(Y2,(YLIMIT)+2)YLIMIT
  [23] PLOT←(NPLOTS<II+1)/END
  [24] C[II:] CONVERT S[II:]
  [25] YLIM←YLIMIT[II:]
  [26] SET VIEWPORT CORNER TO CORNER,SIZE TO SIZE
  [27] 'ECPLOTMOD,DATA[II:]
  [28] XL[II:] LABEL YL[II:]
  [29] →PLOT
  [30] END:LEN3
  [31] LENTO
  [32]

```

```

VCONVERT[]V
V C CONVERT S
[1] C[1]+C[1]*273
[2] CORNER-C[1],C[2]+C[2]*283.6
[3] S[1]+S[1]*273
[4] SIZE-S[1],S[2]+S[2]*283.6
V
V EGNPLOTMOD[]V
V WIN EGNPLOTMOD DATA
+OK*11=CPDATA
[1] DATA+DATA VS10DATA
[2] OK:USING SCREEN,BUFFERED
[3] +SKIP*10=6.WIN
[4] SET VIEWPORT CORNER TO 600 400 ,SIZE TO(Φ2ΦWIN)*.CSZ[CHARSIZE DEFN:]
[5] SKIP:((L/DATA[1]),I/DATA[1]) EGMAXIS YLIM
[6] I+2
[7] LOOP +DATA[1:1] WITH DATA[1:I]
[8] ΔV2S
[9] MOVE TO DEFN
[10] +(1+DATA[1]) WITH 1+DATA[1:I]
[11] +(1+5 6 7)[1+5] 2+I] ΔP2A TO DEFN
[12] ΔV2S
[13] ADRH
[14] +((1+DATA)≥I+I+1)/LOOP
[15] ANMODE
[16]
V
V LABEL[]V
V XLAB LABEL YLAB:I,J
USING SCREEN
[1] I+VIEWPORT DEFN
[2] SET CHARSIZE TO 2
[3] STRING XLAB AT 1+CURSOR
[4] J+0
[5] MOVE TO 1+CURSOR
[6] USING CHARACTERS
[7] LOOP:→XIT*J+YLAB
[8] STRING YLAB[J+J+1]
[9] MOVE 0 1
[10] +LOOP
[11] XIT:ANMODE
[12]
V

```



```

7SENDONEN
7 DSW-SETDSN DIPFG
[1] ACC=HB.A3H01.A' (V1+DAL), ' '
[2] A--CHANGE TO FORM ANOTHERS PLOTS
[3] 'LIMIT RESPONSES TO 18 CHARACTERS.'
[4] ' '
[5] 'ECC QUALIFIER NAME?'
[6] 'GIVE A QUALIFIER IF YOU WANT ONE, ELSE HIT CARRIAGE RETURN.'
[7] QUAL=
[8] 'ECC NAME?'
[9] NAME=
[10] --(C+QUAL)/A
[11] DSP=ACC.NAME
[12] --END
[13] A:DSP=ACC.QUAL,' ' .NAME
[14] END:--(DIPFG=0)/0
[15] ' ' CHK 'SVG' TRY 'SV DSP=HB.A3H01.P379021.APL.GRAPELCS.DIP,UNIT=3330,VOL=000062,DISP=MOD '
[16] SVG=(V1+DAL), ('9+QUAL'), ' ' .NAME
[17] ' ' CHK SVG
[18] SVG=
[19] ' ' CHK SVG

```



```

VANOVA[1]V
V ANOVA D:IO
[1] DIO=1
[2] TEX 4
[3] SOURCE DF SS MS P-FIXED
[4]
[5] N=(DIM+D)-1
[6] T=((R*(2*N)+2*X+(REPS+DIM[1])/2),4)PO
[7] CT=((N-1)PO) SS D
[8] T[R; 2 3]=((*/DIM)-1),((N+1)PO1) SS D
[9] + (REPS=1)/REP
[10] T[1; 2 3]=((REPS-1),((N+1)PO1) SS D
[11] REP:D=+/[1] D
[12] SUMS=D
[13] DIV=DIM
[14] DIM=1+DIM
[15] V=[(2*(N+1)-N)*, |S|*(2*N-N)*, S*(2*N)-1)PO1
[16] V[1; (2*N)-1]=V[1; (X*.X)+(10X)*, 210X)*X*.X)10X=+/[1] V
[17] I=1
[18] CALC:T[I;K; 2 3]=((V[1;I]=1)/DIM-1), (V[I;I] SS D)*REPS
[19] +((2*N)>I+1)/CALC
[20] T[3;3]=T[3]-CT
[21] + (N=1)/ONE
[22] I=2
[23] CONT:DV=(MPO), (X*(-CT)*V, AS)^(CT-V[I;I])V, AS+V[I;I-1]), (R-(I+K-1))PO
[24] T[I;K; 3]=T[I;K; 3]-+T[3;3]*DV
[25] +((2*N)>I+1)/CONT
[26] ONE=-(REPS=1)/REPOH
[27] T[P-1;2]=T[R;2]-+/[1] T[1(R-2);2]
[28] T[R-1;3]=T[R;3]-+/[1] T[1(R-2);3]
[29] REPOH:T[1(R-1);4]=T[1(R-1);3]*T[1(R-1);2]
[30] I=1
[31] PRNT:T[I;K;1]=10*V[I;I]
[32] +((2*N)>I+1)/PRNT

```

```

VANOVA[33]V
[33] L2=0=2*V[1]
[34] L=L2/2 10 0'ERROR TOTAL
[35] V=((-V/L2),0)V=ASORT V[1]
[36] V=V[1] L
[37] R=1+V
[38] R=R-1
[39] +(0=V[1:1])/OUT
[40] T[N:1:12]=T[1:1+12]*T[N:1+12]
[41] T[N:4:3]=T[N:3]*T[N:2]
[42] +(0=V[1:4])/MSG
[43] F=T[1:4]*T[N:4]
[44] T=F
[45] T=1 1 +T
[46] (1 0 +V),(9 0 . 12 4 . 12 4 . 12 4)WT
[47] -MEANS
[48] OUT:F=T[4]*T[N:4]
[49] T=(0 1 +T)*F
[50] V,(9 0 . 12 4 . 12 4 . 12 4)WT
[51] MEANS:-((0=V[1:2])/END
[52] -)
[53] END:TWOM
[54] -(1=1+DIV)/R2
[55] R1+3
[56] -COMP
[57] R2:R1+4
[58] ' '
[59] ' '
[60] COMP:'ENTER MULTIPLE COMPARISON PROCEDURE'
[61] 'CHOICES ARE: '
[62] 'TUNE2 SCHE2L SCHE2C BONF2L BONF2C'
[63] -)
[64] MSG:'ERROR SUMS OF SQUARES IS 0'

```

```

VSS[0]V
S=Y SS P:DIM:K:ZEROS:ONES
  + (X=ONES-K-ZEROS*(Y=0))/(K-DIM+P)/4
[1] R+=[(10)ZEROS] R
[2] + (0*ZEROS-1*ZEROS)/2
[3] R+R*2
[4] R+R/R
[5] + (0<ONES+ONES-1)/5
[6] S=R*Y/(Y=0)/DIM
[7]

```

```

VASORT[0]V
R=ASORT X:IO:I
[1] IO+1
[2] R+ 0 10 p'
[3] + (0 1 *ppX)/SC,VEC
[4] 'CAN NOT DO MATRICES'
[5] +
[6] SC:X-1+X
[7] VEC:I+0
[8] + ((pX)<I-I+1)/0
[9] R+R.[1] 10+((26p10)*X[I])/('ABCDEFGHIJKLMNPOQRSTUVWXYZ'
[10] +VEC+1

```

```

VTWOMB[0]V
TWOMB
[1] NEHA+(-/[1] SUMS)*+/(1+DIV)
[2] NEHB+(-/SUMS)*+/(1+DIV),('1+DIV)

```

```

VTUNE2[[]]V
V TUNE:Q,DF,MSUB,LB,UB,DELTA,DELTA
[1] ' '
[2] '***TUNE***'
[3] ' '
[4] DF+(DIV[3],T(R1):1)
[5] ' FACTOR A'
[6] Q-1' ASK 'ENTER Q AT THE 1-a LEVEL WITH DF',(VDF),' '
[7] ' '
[8] DELTA-Q*(T(R1):3)*(1/(2+DIV)))0.5
[9] LAYOUT DIV[3]
[10] MSUB+HEA[COL1]-MENB[COL2]
[11] LB+MSUB-DELTA
[12] UB+MSUB+DELTA
[13] ' T '
[14] (12 0 . 12 0 . 12 4 . 14 4)COL1, COL2, LB, UB
[15] ' '
[16] ' FACTOR B'
[17] DF+(DIV[2],T(R1):1)
[18] Q-1' ASK 'ENTER Q AT THE 1-a LEVEL WITH DF',(VDF),' '
[19] DELTA-Q*(T(R1):3)*(1/(DIV[1,3]))0.5
[20] LAYOUT DIV[2]
[21] MSUB+HEA[COL1]-MENB[COL2]
[22] LB+MSUB-DELTA
[23] UB+MSUB+DELTA
[24] ' '
[25] ' T '
[26] (12 0 . 12 0 . 12 4 . 14 4)COL1, COL2, LB, UB
V

VLAYOUT[[]]V
V LAYOUT T:I:S
COL1=COL2+10
[1] I=0
[2] LP:=(T-I+1)/OUT
[3] S=(T-I)/I
[4] COL1=COL1,S
[5] S=I+17
[6] COL2=COL2,S
[7] -LP
[8] OUT:COL1=((COL1),1)COL1
[9] COL2=((COL2),1)COL2
[10] V

```

```

V DSTAT[11]
  R=(MAX-X*0X1)-MIN*(X-X*AX)[1]
  SD=(VAR*(+/(X-MEAN)*(N+2)+(N+0X)-1)*0.5
  MD=(+/(X-MEAN)*N
  MED=0.5*(X*([N+2],1+[N+2]
  + (N>0MODE*(0V)0(1M)S1)/V*(V-M*(V+X)/(X*0.5X))/7
  MODE=10
  'SAMPLE SIZE
  'MAX
  'MINIMUM
  'MINIMUM
  'R
  'MEAN
  'VARIANCE
  'STANDARD DEVIATION
  'SD
  'MEAN DEVIATION
  'MED
  'MODE
  'MODE

```

```

7 LILLIEX(0)
7 LILLIEX X:QIO:M:P;DELTA:D;DLILLY:SSTAR:R1:R2;S:A:B;Q:DF
[1] 10+1
[2] M*(+/X)+pX
[3] F*(1-X[AX])W
[4] DELTA=((10X)+pX)-P,P*((10X)-1)+pX
[5] D=f(0(2,pX)pDELTA
[6] DLILLY=f/DELTA
[7] SSTAR=+/10
[8]
[9] LILLIEFORS MS TEST FOR EXPONENTIAL DISTRIBUTION WITH UNKNOWN MEAN
[10] D* = 'DLILLY'; N = '10X
[11] SEE JASA 64:387-389 FOR TABLES
[12]
[13] FINKLESTEIN AND SCHAFER S< TEST FOR EXPONENTIAL DIST. WITH UNKNOWN MEAN
[14] S* = 'SSTAR'; N = '10X
[15] SEE MANN, SCHAFER, SINGPURWALLA, METHODS FOR STATISTICAL ANALYSIS OF RELIABILITY AND LIFE DATA PAGE 337 FOR S* TABLE
[16] R1=L(0X)+2
[17] R2=(0X)-R1
[18] S=(010X)*X[AX]-(0,1+X[AX])
[19] A=(+/R1+S)+R1
[20] B=(+/R1+S)+R2
[21] C=A+B
[22]
[23] THE FERENC-RINGER-CHEDENKO Q-STATISTIC IS
[24] Q= 'Q
[25] DF=(2*R1),(2*R2)
[26] TO BE COMPARED WITH P WITH 'DF,' DF AT THE 1-(0+2) LEVEL

```

```

WEIBULL[ ]
WEIBULL X:UO;I;N;K;D;L;C;S
UO=1
'ZEIBULL TEST OF FIT'
'CONSTANTS K AND PERCENTILES FOR S CAN BE FOUND '
' IN MANN, SCHAFER, AND SINGPURWALLA PAGES 342-347'
I=0
N=O
K=10
X=X[AX]
D=(1+X)-(-1+X)
LP:=(N-I-1)/OUT
K=K.s'' ASK 'ENTER K WITH N= ',(N), ' AND I= ',I
-EP
OUT:L-D*K
C=1+(N+2)
C=(C-1)+L
S=(+C)*(+/L)
'S= 'S

```